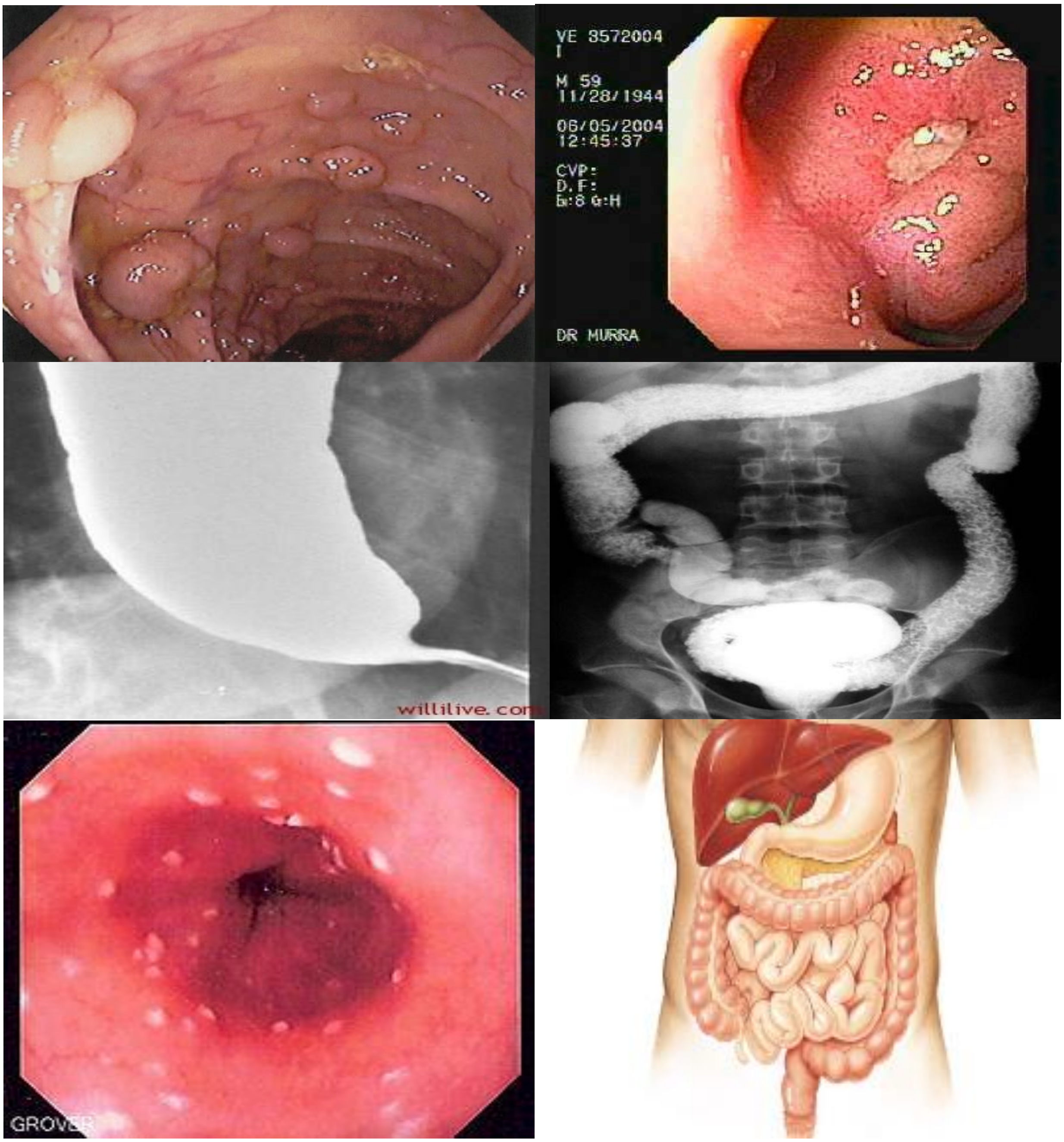
GASTROENTEROLOGY



Dr. Ibrahim Ashour Hamed

Imbaba fever hospital

ESOPHAGEAL DISORDERS

Infectious esophagitis

Key facts

1- Most commonly seen in immunosuppressed patients and rarely encountered in immunocompetent hosts
2- Fungal and viral diseases are the most common agents in immunosuppressed patients

Incidence → 30% of HIV patients

Risk factors

1- HIV
2- Chemotherapy
3- Immunosuppressive therapy

Etiology

1- Fungal esophagitis

- Candidiasis esp. candida albicans → the most common infectious disease of the esophagus in HIV patients (70%)
- Histoplasma capsulatum → rare

2- Viral esophagitis

- CMV → the most common cause of esophagitis in HIV patients [the risk is low in patients with CD4 > 100]
- VZV
  - Can cause a devastating esophagitis in severely immunocompromised hosts
  - Rare in immunocompetents, but can be seen in children with chicken pox or adults with herpes zoster
- HSV → uncommon
- EBV, human papillomavirus → extremely rare

3- **Bacterial esophagitis** (rare)

  - Mycobacterium avium complex and tuberculosis
  - Nocardia, actinomyces and lactobacillus

4- **Idiopathic esophagitis**

  - Idiopathic esophageal ulceration is common in patients with a CD4 < 50

Clinical presentation

1- **Candidiasis**

  - Dysphagia is the most common symptom
  - Thrush often present
  - Odynophagia, fever, nausea and vomiting are less common

2- **Cytomegalovirus**

  - Odynophagia and chest pain are the most common symptoms
  - Dysphagia is uncommon
  - Fever, nausea and vomiting may be present

3- **Herpes simplex virus**

  - Most commonly present with both dysphagia and odynophagia with fever and chest pain

4- **Varicella zoster virus**

  - As HSV
  - The characteristic skin lesions of chickenpox in children and zoster in adults may help diagnosis

5- **Idiopathic esophageal ulceration**

  - Severe odynophagia in almost all patients
  - Dehydration and malnutrition

N.B. physical exam. → may be fever and orthostatic hypotension from dehydration

Diagnostic testing

1- **CBC** → ↑ WBCs may suggest infection, but this finding is variable in patients with immunodeficiency

2- **CD4 count** → determines the most likely pathogen in HIV patients

CD4 count	Typical organisms involved
>200	HSV, VZV
100 – 200	Candida, HSV
50 – 100	Candida, CMV, HSV
<50	Idiopathic esophageal ulceration

3- Endoscopy (EGD) and biopsy

- Indications
  - Failure of empiric antifungal therapy for suspected candida esophagitis
  - If symptoms include weight loss, dehydration or fever
- Value
  - Can distinguish between the types of esophageal infections

Type	Gross	Histology
Candidiasis	Multiple adherent, white or yellow "cottage cheese" plaques	Yeast or budding hyphae
CMV	Large well demarcated ulcers	Giant cells with cytomegaly and large, ovoid, or pleomorphic nuclei with basophilic inclusions. (owl's eyes) - Immunohistochemistry is more specific than standard staining techniques
VZV	Multiple vesicles and confluent ulcers	Cytology is difficult to distinguish from HSV and often requires immunohistochemistry or culture
HSV	Early → small superficial ulcers Late → diffuse esophagitis	Giant cells and ground glass nuclei
IEU	Large well circumscribed ulcers	To exclude infectious causes

Treatment

1- Empiric therapy

- Many clinicians recommend an empiric course of fluconazole to treat candida esophagitis in patients with AIDS and dysphagia, but without other symptoms

2- Candidiasis

- 1st line therapy → fluconazole 200 mg loading dose followed by 100 mg daily for 5 – 10 days

- In patients with azole resistant candida
    - ↑ the dose of fluconazole or give
    - I.V. amphotericin
- Severe refractory cases may not improve until treatment of HIV is undertaken to ↑ CD4 count

3- **Cytomegalovirus**

- Ist line therapy → I.V. ganciclovir 5 mg/kg every 12 h until healing occurs usually up to 1 month (if the patient is not pancytopenic)
- Alternate therapy → I.V. foscarnet 60 mg/kg every 8 h
- Approximately 30% of patients relapse

4- **Herpes simplex virus**

- 1st line therapy
    - I.V. acyclovir 5 mg/kg every 8h for 7-14 days or
    - Oral acyclovir 400 mg 5 times a day for 14-21 days
- Alternate → famciclovir, valacyclovir and ganciclovir

5- **Varicella zoster virus**

- I.V. acyclovir 5 mg/kg every 8h for 7-14 days

6- **Idiopathic esophageal ulceration**

- Oral corticosteroids, or I.V. if oral intake can't be tolerated
- Fluconazole is given twice weekly for prophylaxis against candida
- In refractory cases → thalidomide can be used

Prophylaxis

1- **1ry prophylaxis**

- Recommended only for CMV in patients with CD4 < 100 mg, although there is no evidence that it ↓ the incidence of gastrointestinal disease
    - Long term oral ganciclovir → discontinue if CD4 count ↑ > 100-150 and HIV RNA has suppressed

2- **Secondary prophylaxis** in patients with multiple recurrences

- Candida → fluconazole 100 mg weekly
- HSV → acyclovir 600 mg orally daily

3- **In refractory cases** → thalidomide can be used

Gastroesophageal reflux disease

Definitions

1- **Gastroesophageal reflux:**

- A motility disorder of the lower esophageal sphincter characterized by regurgitant episodes of acid- pepsin reflux from the stomach to the esophagus through an incompetent sphincter.
- This may or may not produce symptoms.
- The most common symptoms are heart burn, regurgitation, chest pain and dysphagia.

2- **GERD:** include the constellation of symptoms and consequences to the esophagus from reflux damage

Etiology and pathogenesis [failure of ant-reflux mechanisms]

1- The resting LES **pressure** is low and fails to ↑ when lying flat

2- ↓ esophageal clearance of acid due to poor esophageal **peristalsis**

3- Delayed gastric **emptying**

4- **Hiatus hernia** may impair the pinchcock mechanism of the diaphragm

5- The lower esophageal **tone** fails to ↑ when intra-abdominal pressure is increased by tight clothes or pregnancy

Unstable LES: recurrent inappropriate relaxations without stimulus (it is the commonest cause of 1ry GERD)

Hypotensive LES: less common, occur as 1ry disease or as a part of general disease as progressive systemic sclerosis (occasionally, PSS present as GERD before skin manifestations)

Increase LESP	Decrease LESP
- Gastrin	- Secretin
- Pitressin	- Cholecystokinin
- Angiotensin 11	- Glucagon
- Cholinergics (e.g. bethanechol)	- VIP
- Gastric alkalinization	- Progesterone (CCP)
- Metoclopramide	- Theophylline
- Anticholinesterases	- Gastric acidification
- Protein meal	- Fatty meals
- PGf 2α	- Chocolate (xanthines)

	- Carminatives (spearmint,peppermint) - Smoking - Ethanol - α- adrenergic antagonists - beta adrenergic agonists - Anticholinergics - Calcium channel blockers - Nitrates - PGE2, PGA2 - Morphine, meperidine - Diazepam, other benzodiazepines

Clinical picture

Typical cases:

1-Heartburn:

- Felt as substernal burning pain (recurrent) radiating upward to the throat and to the back of tongue, this worse after eating
- Ingestion of antacids usually relieves symptoms within 5 minutes.

2-Regurgitation:

- Reflux of sour or bitter material into the mouth usually at night while lying down or when bending over.
- May cause nocturnal aspiration awakens the patient.

Atypical cases:

1- Chest pain (angina like):

- Simulate cardiac pain in location, radiation, character.
- Should be investigated first as a cardiac case until proved otherwise.
- Due to acid induced irritation of the nerve endings or GERD induced esophageal spasm or GERD induced angina pectoris.

2- Pulmonary symptoms: (may be the only manifestation of GERD esp. at night & in children).

- Chronic cough, asthma, wheezes, recurrent aspiration pneumonia, haemoptysis, hoarseness of voice or posterior laryngitis
- Cause → direct aspiration of acid or vagus mediated neural reflexes

- Radionuclide scintiscanning of the lungs → may document pulmonary aspiration following placement of technetium 99m-sulfur colloid in the stomach, but negative results don't exclude

3- **Chronic hypochromic anaemia:**

- Intermittent small bleeds may occur due to oesophagitis or distal oesophageal erosions without the patient's Knowledge
- May be too small to cause manifest hge but enough to cause anaemia of obscure origin
- Endoscopy should be routine investigation in any case of hypochromic anaemia of obscure origin

4- **Oropharyngeal symptoms:**

- Dysphagia → due to stricture or inflammation and oedema
- Odynophagia → due to severe oesophagitis
- Waterbrash → sudden filling of the mouth with clear, slightly salty fluid which comes in large amounts and secreted by the salivary glands in response to GERD.
- Halitosis, dental caries, sore tongue, otitis media (rare).

5- **Other symptoms:**

- Sleep apnea
- Day time sleepiness
- Poor sleep/insomnia

Complications

1- **Esophageal strictures (11%)**

- Cause: fibrosis of the deep esophageal ulcers or inflammation below the mucosa (esophagitis)
- Risk factors:
  - Prolonged GERD
  - Reflux while supine
  - NGT
  - Treated achalasia
  - Scleroderma
  - Postgastrectomy and hypersecretory states

- Site:
  - Usually in the distal 1/3 of the esophague
  - In Barrett's esophagus, may be in the middle 1/3
- Presentation → heart burn disappears or ↓ and replaced by dysphagia if esophageal intraluminal diameter ↓ to < 12 mmHg
- Schatzki's ring → ring stricture in the distal esophagus at the E-G junction

2- **Esophageal ulcers and bleeding**

- Deep esophageal ulcers (in small %) → hematemisis or melena
- Ulcers should be biopsied prior to treatment to exclude metaplastic Barrett's epithelium
- Bleeding usually self limited or respond to intensive medical therapy

3- **Barrett's esophagus (20%):**

- Age: usually > 40 yr & in patients with night time GER
- Definition: chronic reflux esophagitis leading to replacement of the normal squamous epithelium of the distal esophagus with metaplastic specialized columnar epithelium called Barrett's epithelium
- Complications: Leads to peptic ulcer and strictures and adenocarcinoma
  - Strictures characteristically found in the mid to lower esophagus with squamous epithelium above and columnar epithelium below the stricture
  - Premalignant → adenocarcinoma of the lower esophagus and gastric cardia (Barrett's cancer: 3-9%)
  - The malignant lesion should be suspected in any patient with mid esophageal narrowing and stricture formation, but may be present without these findings
- Barrett's epithelium: consists of a complex mixture of varying cell types, glands and surface architecture that is normally seen in the small bowel with varying degree of atrophy
- Subclassified as short segment < 2 cm, long segment > 2 cm
- Surveillance for malignancy:

- Periodic multiple endoscopic biopsies (EGD) + brush cytology
- If low grade dysplasia → every year
- If high grade dysplasia → every 3-6 mo, some suggest therapy and/or surgery

4- **Laryngeal carcinoma:** due to prolonged irritation of the larynx by repeated aspiration

5- & 6- **Anemia and pulmonary manifestations** ®

Investigations

1- Most patients with classic symptoms of GERD (heart burn or regurgitation) can given an **empiric trial of medical therapy** without further investigations

2- Further investigations may be required in **atypical presentation** with suspicion of GERD to establish diagnosis and detect severity and extent

3- **Upper endoscopy**

- Indications of endoscopy + mucosal biopsy:
  - Refractory symptoms
  - Atypical symptoms
  - Odynophagia and dysphagia
  - Suspicion of Barrett's esophagus (GERD > 5 yrs)
- Diagnose reflux esophagitis in 50% (not motility disorder)
- Diagnose peptic ulcer of the lower end of esophagus or Barrett's esophagus
- Diagnose associated lesions as dudenal or gastric ulcers or hiatus hernia
- Mandatory during bleeding
- Mucosal biopsy should taken even if the mucosa is normal (esophagitis is deep)
- Findings of esophagitis by endoscopy:
  - Mild → erythema and edema of the mucosa with obliteration of small linear blood vessel, mild friability and increased irregularity of 'Z line

    - Moderate to severe → round and longitudinal superficial ulcers or erosions, diffusely hemorrhagic mucosa with exudates, deep punched out esophageal ulcers and strictures
- Endoscopic grading of GERD:
    - Grade 0: macroscopically normal esophagus; only histological evidence of GERD
    - Grade 1: one or more non-confluent lesions with erythema or exudate above GE junction
    - Grade 2: confluent, non-circumferential, erosive & exudative lesions
    - Grade 3: circumferential erosive & exudative lesions
    - Grade 4: ulceration, stricture or Barrett's esophagus

4- **Barium swallow and upper GI series**
- May diagnose esophagitis (double contrast studies)
- May diagnose hiatus hernia
- Strictures usually have smooth tapered appearance
- Exclude anatomic causes of dysphagia

5- **Prolonged PH monitoring** [Ambulatory PH-metry]
- The gold standard for measurement of acid GERD
- Indicated if endoscopy –ve or symptoms are atypical
- This test monitor esophageal PH for 24 hr
- PH that denotes acid reflux < 4
- However, since a normal amount of GERD does occur, the total duration of all reflux episodes should > 5% of the total monitoring time in order to diagnose a pathological GERD

6- **Esophageal manometry**
- Indicated in atypical symptoms and before antireflux surgery
- Limited use
- Poor test in predicting GERD unless the LES pressure < 6 mmHg

7- **Wireless PH monitoring** [Brano device]: Prolonged monitoring (2 - 4 days)

Treatment

1- **Dietary and life style changes** [50% will respond]

- Elevation of the head of the bed
  - Esp. for patients with regurgitation
  - May be achieved by the placement of 15.2 cm (6-in.) blocks under the head of the bed or 15.2 cm foam-rubber wedge in place of or under the pillow
- Avoid
  - Smoking
  - Alcohol
  - Fatty and fried foods
  - Chocolate
  - Larg meals that would distend the stomach
  - Tomato products
  - Citrus juices and fruits
  - Coffee, tea and carbonated beverages
  - Carminatives (spearmint, peppermint)
- Encourage
  - High protein, low fat diet → because it ↓ LES pressure and ↑ gastric emptying time
  - 3 small to moderate sized nutritionally balanced meals
  - The evening meal should be light and easy to digest
- No eating: 4-5 hr prior to sleep
- Weight loss: if overweight
- Avoid: tight belts or girdles → ↑ intra-abdominal pressure
- Avoid drugs that ↑ GERD [↓ LES pressure and esophageal clearance]
  - Progesterone
  - Beta-adernergic agonists
  - Anticholinergics
  - Nitrates
  - sedatives/opiates
  - Ca channel blockers
  - Tranquilizers
  - Antihistaminics
  - Theophylline

2- Pharmacologic therapy

- Antacids
    - Every 2 hr is recommended
    - The most effective: combination of magnesium and aluminum hydroxides
    - In renal failure: give only aluminum hydroxide containing antacids, as magnesium may accumulates in the blood
    - In severe sodium restriction: give low sodium preparation (e.g. Riopan)
- Drugs decreasing gastric acid output [H2 blockers]
    - Usually effective in mild to moderate GERD
    - Not effective in healing erosive esophagitis
    - H2 blockers have very limited acid suppressive ability at times of eating
    - Rantidine (Zantac): 150-300 mg q 12 hr
    - Famotidine: 20-40 mg at h.s.
- Proton pump inhibitors
    - Action: they inhibit gastric H – K Atpase
    - Effect: extremely effective in inhibition of gastric acid secretion for 19-24 hr and allow the gastric PH to ↑ > 4 or 5 thus eliminating also the pepsin activity
    - Effectively heal erosive esophagitis
    - Side effects → minor headaches, diarrhea and nausea, ↓ Ca absorption, so if long term use (years) give Ca supplements
    - Preparations: Omeprazole: 20-40 mg (q.d or bi.d) & Lansoprazole: 15-30 mg (q.d or bi.d)
    - All Ppi most effective if taken 15-30 min. before breakfast or dinner
- Drugs ↑ LES pressure and esophageal clearance [prokinetic]
    - Metoclopramide HCL:

      © 10-20 mg q.i.d 15-30 min. a.c and h.s

© cross BBB (10%): → somnolence, lassitude, restlessness, anxiety, insomnia and rarely extra pyramidal reactions

© ↑ prolactin leading to galactorrhea

- Domperidone

  © Successful in GERD and not cross BBB

- Cisapride:

  © 10 mg 4 times daily before meals and at bed time

  © Not available now → cardial arrythmia

- Drugs that enhance mucosal resistance

  - Sucralfate

    © An aluminum sucrose polysulfate shown to be effective in healing duodenal ulcers due to its cyto protective action

    © Not highly effective in esophagitis, but suspension form gives symptomatic and possibly therapeutic benefit to patients with erosive esophagitis

    © Dose: 1 gm 1-4 times daily

  - Prostaglandin analogs [misoprostol]:

    © Effective in peptic ulcer but not highly effective in GERD

3- The results of maintenance therapy

- Patients continued with Ppi + domperidone until the endoscopic lesions clear up (usually in 4 – 6 weeks) and then the patient maintained on one of them in 1/2 the initial dose either on demand basis or on long term basis according to response
- 20 mg omeprazole maintenance dose can relief severe esophagitis (the dose can ↑ to 40 mg)
- 90% had recurrence of esophagitis within 6 months → indicating some form of chronic treatment

4- Surgical treatment [Nissen Fundoplication]

- Ant-reflux surgery done by laparoscope
- Esophageal manometry: is done before surgery for appropriate selection

- Indications: severe cases with complications such as non healing or bleeding ulcer or refractory stricture
- Principle: the gastric fundus is warraped around the abdominal esophagus with repair of hernia if present

5- **Treatment of esophageal peptic strictures**

- Intensive medical therapy: relief symptoms in some patients
- Savory dilators: passed over a guide wire or inflatable balloon dilators with endoscopic guidance
- Endoscopic balloon dilators
- Surgery:
    - indicated: for the 15-40 % in whom dilatation and medical therapy fail
    - pre or intra operative dilatation combined with nissen fundoplication
    - if the stricture can't be dilated or too extensive → resection and end-to-end anastomosis or interposition of a segment of colon or small bowel may be used

6- **Treatment of Barrett's esophagus**

- Intensive medical therapy: with high dose PPIs used in most patients but regression of this metaplastic change has not been documented
- If severe dysplasia → Esophagectomy or mucosal ablation therapy
- Mucosal ablation may be accomplished by
    - endoscopic mucosal resevtions
    - photodynamic therapy followed by laser ablation
    - laser or bipolar heater probe cautery
- These procedures available only in special centers

GERD	Myocardial ischemia
Burning pain produced by bending, stooping or lying down	Compression or crushing pain
Pain seldom radiates to arm	Pain radiates into neck, shoulder and both arms
Pain precipitated by drinking hot liquids or alcohol	Pain produced by exercise
Relieved by antacid, ↑ by nitrates	Relieved by rest and nitrates
No dyspnea	Dyspnea may present

Eosinophilic esophagitis

Definition

1- It is a **clinicopathologic disease** characterized by
    - Symptoms of food impaction and dysphagia in adults and feeding intolerance or GERD in children
    - > 15 eosinophils/HPF on pathologic examination
    - Exclusion of other disorders with similar clinical or pathologic findings
        - GERD
        - Parasitic and fungal infections
        - Crohn's disease
        - Allergic vasculitis and other connective tissue diseases

2- Although eosinophilic infiltration of the esophagus can be seen 2ry in association with other conditions such as GERD, eosinophilic esophagitis is now recognized as a **1ry diagnosis**

Risk factors

1- There is a reported association in **children** with a history of asthma, allergic rhinitis, eczema and food or environmental allergies

2- There is a reported association in **adults** with eosinophilic gastroenteritis and peripheral eosinophilia

Pathogenesis [unknown]

1. The disease may originates from an **immune mediated response** to a swallowed allergen
2. Once eosinophils have infiltrated the esophageal mucosa, their presence appears to trigger a self sustaining cascade of **inflammatory mediators**

Clinical presentation

1. **Age** → all age groups, but usually either in early childhood, adolescence or before the 4th decade of life
2. **Sex** → males comprise 70% of cases
3. **Symptoms**
    - The most common symptoms → dysphagia, heartburn and chest pain
    - Less common symptoms → food impaction or symptoms consistent with esophageal dysmotility
    - Patients may have a diagnosis of GERD but have failed high dose PPIs
    - Any of risk factors listed above may be present
4. **Signs** → no signs are specific to the disease

Complications [from chronic inflammation]

1. Proximal esophageal strictures
2. Mucosal rings
3. Esophageal ulceration
4. Esophageal polyps
5. No esophageal metaplasia or malignancy have been reported even with advanced disease

Differential diagnosis of esophageal eosinophilia

1. GERD
2. Eosinophilic esophagitis
3. Eosinophilic gastroenteritis
4. Crohn's disease
5. Connective tissue disease
6. Hypereosinophilic syndrome
7. Infection
8. Drug hypersensitivity response

Investigations

1- **CBC** → peripheral eosinophilia esp. in children

2- **EGD with biopsies**

- Gross mucosal abnormalities found in > 50% of cases
  - Longitudinal furrowing and shearing
  - Friability and edema
  - Whitish exudates and raised white specks
  - Crepe paper mucosa and narrow caliber esophagus
  - Felinization and transient or fixed rings
- Biopsy should be obtained regardless of the gross appearance of the esophageal mucosa (in a study of 381 children with EE 30% had a grossly normal esophagus)
- Biopsy should be taken from the stomach and duodenum to determine whether the disease is confined to the esophagus or is a manifestation of another process such as eosinophilic gastroenteritis or IBD

3- **Esophageal manometry**

- Patients have normal PH monitoring of the distal esophagus in contrast to GERD

4- **Barium swallow**

- Not routine study in diagnosis of this disease, but may add further data regarding anatomy and assessing for dominant strictures

5- **Allergen skin testing** → suggested by some physicians to avoid potential precipitating foods or allergens

Treatment [No universally accepted treatment]

1- **1st line : topical corticosteroids**

- Fluticasone is used
- Patients instructed to swallow rather than inhale the medication
- Relief of dysphagia is expected within the initial week of treatment

2- **2nd line: systemic corticosteroids**

- Indicated when urgent symptom relief is required as in severe dysphagia, dehydration, weight loss or strictures

- Have significant benefit in pediatric patients, but symptoms recur quickly on cessation [poor treatment option]

3- 3rd line : mepolizumab

- It is a humanized anti-IL5 antibody
- It is effective in improving the clinical and pathological features of the disease
- May replace those listed above if future studies demonstrate its safety and efficacy in adults and children

4- Lifestyle/Risk modification

- Avoidance of known food and environmental allergens → may provide relief in patients with EE
- In one study, 26 of 35 patients showed significant improvement clinically and histologically after initiating a diet free of the 6 most common allergenic foods (dairy, eggs, wheat, soy, peanuts, fish/shellfish)
- Elemental amino acid based formulas → extremely effective in the pediatric patients but usually need gastrostomy or NGT for administration and are quite costly

5- In patients with significant dysphagia and stricture

- Esophageal dilation relieve symptoms for several months [despite the risk of perforation, the procedure is relatively safe]

Esophagitis

Causes

1- Reflux esophagitis (see GERD)
2- Infectious esophagitis
3- Eosinophilic esophagitis
4- Pills induced esophagitis

- Results from drugs as tetracycline, iron, NSAIDs, KCL tablets
- Prevented by drinking sufficient fluid > 120 ml with oral medications

Esophageal strictures

Etiology

1- **Peptic strictures**

  - Relatively common, occurring in about 10% of patients with GERD
  - Site → typically in the distal esophagus, often just proximal to the squamocolumnar junction

2- **Schatzki's rings**

  - Can be associated with GERD, pill esophagitis and hiatal hernias
  - Site → in the distal esophagus at the squamocolumnar junction
  - By definition, schatzki's rings have squamous mucosa on the proximal aspect and gastric columnar mucosa on the distal aspect
  - Intermittent, nonprogressive solid food dysphagia can occur, sometimes termed " steakhouse syndrome"

3- **Plummer-Vinson syndrome**

  - Characterized by anemia, upper esophageal webs and dysphagia
  - Typically seen in middle aged women

4- **Other causes of esophageal narrowing**

  - Caustic ingestion
  - After band ligation for varices
  - Esophageal infections
  - Repetitive vomiting
  - Esophageal neoplasms
  - Radiation therapy
  - Pill induced esophageal inflammation "pill esophagitis"
  - Esophageal trauma e.g. instrumentation, NGT
  - Crohn's disease

Risk factors

1- GERD
2- History of esophageal infections
3- Crohn's disease

History

1- Onset and duration of symptoms
2- Association of dysphagia with types of food
3- Description of regurgitated material if present
4- History of weight loss
5- History of GERD
6- Evaluation for other risk factors listed above

Physical examination [to assess severity]

1- Weight loss
2- Dehydration
3- Malnutrition

Diagnostic testing

1- CBC → anemia in esophageal inflammation, neoplasia, Plummer-Vinson syndrome

2- Low albumin conc.→ may reflect nutritional deficiency

3- Barium swallow

- Useful test in the workup of suspected stricture, ring or web, esp. when the lesion is subtle and not recognized by endoscopy
- Not recommended as the initial test in new onset dysphagia, as endoscopy provides both definitive diagnosis and therapy of strictures

4- EGD

- Allows direct visualization of stricture, web or rings. Biopsies can be taken to evaluate the etiology and dilation allows therapy of the strictures

Treatment

1- Peptic stricture

- Aggressive acid control with high dose PPIs → can cause regression of the stricture
- Endoscopic dilation often required
- Currently, stent placement is not considered routine for benign strictures (carries the risk of stent migration)
- Surgery, occasionally required if dysphagia not relieved by maximal mediacl therapy

2- **Schatzki's ring**

  - Patients with mild disease → should be advised to chew their food carefully
  - Patients with more severe disease → passage of endoscopic dilator (as they are at increased risk for food bolus impaction)
  - Refractory cases → pneumatic dilation, electrocautery incision or surgical repair
  - All patients should be evaluated for GERD and started on PPIs therapy if indicated

Follow up/monitoring

1- Patients with **Plummer-Vinson syndrome** → have increased risk of developing squamous cell carcinoma of the esophagus

2- However, it is unclear whether they should undergo **screening EGD**

Barrett's esophagus

Definition

1- chronic reflux esophagitis leading to replacement of the normal squamous epithelium of the distal esophagus with metaplastic specialized columnar epithelium called Barrett's epithelium

2- incidence is 20% of patients with GER

Risk factors

1- Age: usually > 40 yr

2- Sex: There is a male predominance.

3- Ethnicity: more common in whites.

4- Obesity: High BMI & intra-abdominal distribution of body fat are strong risk factors.

5- Diet: High vegetable and fruit intake appear to diminish the risk of Barrett’s esophagus, although the mechanism is not known.

6- Reflux Symptoms: night time GERD is strongly associated with Barrett’s esophagus.

7- Smoking & alcohol:

- Some studies have found an association between either smoking or alcohol and Barrett’s esophagus.
- However recent data suggest that consumption of wine actually may protect against Barrett’s esophagus.

Complications

1- Peptic ulcer and strictures

- Strictures characteristically found in the mid to lower esophagus with squamous epithelium above and columnar epithelium below the stricture

2- Adenocarcinoma

- Premalignant → adenocarcinoma of the lower esophagus and gastric cardia (Barrett's cancer: 3-9%)
- The malignant lesion should be suspected in any patient with mid esophageal narrowing and stricture formation, but may be present without these findings

Diagnosis

1- Clinically:

- May be asymptomatic.
- Associated with esophagitis i.e. heartburn, waterbrash, dysphagia, vomiting.

2- Investigations:

- Endoscopy for biopsy: identifying anatomic landmarks is essential to get correct biopsy
  - Level of diaphragmatic crus (usually 40 cm in males, 38 cm in females).
  - Gastroesophageal junction (where the gastric fold fades out into the tubular esophagus).
  - Squamo-columnar junction.
- Histopathology: shows intestinal metaplasia.

- Barrett's epithelium: consists of a complex mixture of varying cell types, glands and surface architecture that is normally seen in the small bowel with varying degree of atrophy

- Subclassified as short segment < 2 cm, long segment > 2 cm

Surveillance for malignancy

1- Since transformation to neoplasia depends more on the degree of dysplasia than on mucosal length, the current practice is to offer the same surveillance regimen to patients with short-segment or long-segment Barrett’s esophagus.

2- **If no dysplasia** → Periodic multiple endoscopic biopsies (EGD) + brush cytology every 3 years by taking 4-quadrant biopsies every 2 cm throughout length of Barrett's

3- **If low grade dysplasia** → every year until no dysplasia on 2 successive occasions. [Give a high dose of PPIs to minimize inflammation that makes pathological interpretation more difficult]

4- **If high grade dysplasia** → every 3-6 mo, some suggest therapy and /or surgery

Treatment

1- **Intensive medical therapy:**

- With high dose PPIs used in most patients but regression of this metaplastic change has not been documented even with anti reflux surgery
- Treatment only indicated for reflux symptoms or strictures

2- **If severe dysplasia:**

- Esophagectomy or
- Mucosal ablation therapy: which may be accomplished by
  - Endoscopic mucosal resections

    © It involves lifting the Barrett's lining and injecting a solution under it or applying suction to it and then cutting it off

    © The lining is then removed through the endoscope

    © Complications: Bleeding or tearing of the esophagus
  - Photodynamic therapy followed by laser ablation

© It uses a light-sensitizing agent (Photofrin) and a laser to kill precancerous and cancerous cells

© Photofrin is injected into a vein and the patient returns 48 hours later

© The laser light is then passed through the endoscope and activates the Photofrin to destroy Barrett's tissue in the esophagus

© Complications: Chest pain, nausea, sun sensitivity for several weeks, and esophageal strictures.

    - Laser or bipolar heater probe cautery

- These procedures available only in special centers

Esophageal cancer

Pathogenesis

1- The median **age** of onset → 69 years.

2- **Sex** → Males are 2 - 4 times compared to females.

3- **Site:**

- Squamous cell carcinoma
    - 10% - 15% → in upper 1/3
    - 35% - 40% → in the middle 1/3
    - 40% - 50% → in the distal 1/3
- Adenocarcinomas → arise predominately in the distal esophagus and are commonly associated with Barrett's esophagus or may extend from gastric carcinoma.

4- Between 5% - 12% of patients with esophageal cancer are found to have synchronous or metachronous aerodigestive tract cancer.

5- Local spread from the lung and thyroid and metastasis from distant cancers may occur but are rare.

6- **Predisposing factors**

- Chronic use of alcohol and smoking are associated with esophageal carcinoma.

- Achalasia
- Barrett's epithelium
    - Recurrent symptoms of GERD seem to increase the risk of esophageal adenocarcinoma by 8 fold
    - Anticholinergic, calcium channel blockers, nitrates, and theophyllines, by decreasing the lower esophageal sphincter tone, increase the risk of adenocarcinomas
    - Obesity → increases intraabdominal pressure and GERD
- Lye and corrosive strictures
- Previous exposure to ionizing radiation
- Head and neck cancer
- Plummer-Vinson syndrome
- Tylosis: hereditary disorder of squamous epithelium with hyperkeratosis of palms and soles
- Celiac sprue

7- **Spread and complications:**

- Direct → adjacent structures.
- Lymphatic → to mediastinal cervical and celiac lymph nodes.
- Hematogenous spread → to lungs, liver, and other organs.
- Esophagobronchial or esophagopleural fistulas may form and manifest as recurrent pneumonia or abscess.
- Erosion into the aorta may result in exsanguination.

8- **Pathology**

- Gross → usually ulcerative which extend around the wall of the esophagus causing narrowing
- Microscopic → usually squamous cell carcinoma, but adenocarcinoma can occur in columnar epithelium of Barrett's esophagus

Clinical features

1- **Progressive dysphagia:**

- The most common symptom.
- For less than a year

    - First with solids then with semisolids and liquids

2. **Substernal pain:**
    - Usually steady
    - Radiating to the back
    - May suggest periesophageal spread of the tumor.
3. Anorexia and profound weight loss → in most patients
4. Iron-deficiency anemia from blood loss from the lesion may be present, but brisk bleeding is rare.
5. Hoarseness → if the recurrent laryngeal nerve is involved
6. If the lesion is obstructive:
    - Patients may aspirate esophageal contents → aspiration pneumonia and pleural effusion.
7. **Mediastinal syndrome**, Horner's syndrome, cervical adenopathy, hpeatoroegalys, boney pain, and paraneoplastic syndromes including hypercalcemia, inappropriate ACTH, and gonadotropins may be present.

Investigations

1. **Barium swallow:**
    - A double-contrast study may be helpful in identifying small, plaquelike lesions.
    - Findings:
        - Irregular filling defect with shouldering sign (ridge or shelf at the superior portion of the tumor).
        - Rat-tail appearance may occur
    - Can not differentiate tumor from a benign peptic stricture
2. **Endoscopy**: with biopsy
3. **CT scan** of the chest and abdomen : detect extent and spread of extramucosal tumor
4. **Endoscopic ultrasonography (EUS):**
    - Most accurate method for evaluating the depth of esophageal cancer invasion and detecting abnormal regional lymph nodes.
5. **PET scan** → may improve the detection of stage IV disease.

6- **Preoperative thoracoscopy and laparoscopy**
    - May help assess extent of local disease as well as the involvement of regional lymph nodes and celiac and perigastric nodes.

Staging and prognosis

1- **TNM classification:**
    - T indicates depth of primary tumor invasion
    - N indicates spread of cancer to regional lymph nodes
    - M indicates distant metastases

2- **T1-2, N0M0** are potentially curable with surgery alone

3- Tumor invasion into serosa (T3) or regional or distant lymph node metastases (T4) are associated with significant reduction in survival.

4- The 5-year survival rate for all patients is approximately 16%.

5- The 5-year survival even with the earliest stages of cancer is only 50% to 80% and with lymph node involvement it drops to below 25%.

Treatment

Options

1- Tumors confined to the esophagus → surgery ± radiotherapy and chemotherapy

2- Inoperable tumors → treated by radiotherapy because squamous carcinoma of the esophagus is relatively radiosensitive (Adenocarcinomas are resistant to radiation therapy)

3- Chemotherapy alone not effective

4- Treatment protocols combining chemotherapy and radiation therapy before and after surgery → offer somewhat better results than singlemodality therapy.

5- Most successful chemotherapeutic agents are:
    - The combination of cisplatin, 5-fluorouracil, paclitaxel, irinotecan hydrochloride, vinorelbine tartrate, and gemcitabine hydrochloride

Surgery

1- **Operation:**
    - Total esophagectomy is the surgical procedure of choice.

- For most lesions, it is preferred to resect the involved portion of the esophagus with wide margins, bring the stomach into the chest, and create an anastomosis with the remaining esophagus.
- Colonic or jejunal segment interposition carries a high complication rate.

2- **Best results** occur in lesions < 5cm of the lower 1/3 [“resectable” tumors in the distal third of the esophagus (T_{1-3} N_1) with pre- and neoadjuvant chemoradiation therapy]

3- **Palliative resection:**

- Alleviate symptoms and allow patients to swallow
- For purposes of palliation, the stomach may be anastomosed to the esophagus in a side-to-side fashion to bypass the obstructed area.

4- **Approach:**

- Large thoracotomy carry very high morbidity and mortality
- Combined abdominal incision and a right thoracotomy is preferred.
- If the lesion is low enough, an abdominal approach may suffice.

Other palliative measures

1- **Mechanical dilatation:**

- By Savary or balloon dilators under endoscopic guidance.
- Should be done slowly (high risk of esophageal perforation)

2- **Tube placement:**

- Indicated if it becomes difficult to maintain a lumen at the area of the tumor
- A stent (plastic or metal) may be placed in the lumen endoscopically.
- These tubes may erode into the esophageal wall, causing ulceration, bleeding, and perforation.

3- **YAG-laser therapy:**

- Effective in palliation of patients with advanced obstructing esophageal tumors.
- These masses may be “pared down” by the laser to open the lumen.
- May be useful in the treatment of very early lesions (more studies n).

4- **Injection necrosis of fungating esophageal cancer:**

  - Intratumoral injection of absolute alcohol or ethylene glycol with endoscopic visualization to “open up” the lumen.
  - If malignant strictures present, it should dilated first

5- These palliative measures are usually **repeated** as needed with progressive, repeated growth of the tumor.

Prevention and surveillance

1- **P**atients with recurrent symptoms of GERD are recommended to have **endoscopy** and biopsies for the diagnosis of Barrett's esophagus.

2- **Stop** smoking and alcohol

3- **Current recommendations** for patients with Barrett's esophagus:

- Low-grade dysplasia → endoscopic surveillance every 6-12 mo
- High-grade dysplasia
  - Substantiate the diagnosis by two different pathologists
  - Then consider esophagectomy or mucosal ablation with photodynamic therapy.

Esophageal motility disorders

Definitions

1- **Swallowing involves 2 types of muscular activity**

- It is initiated by neural impulses from the CNS, controlling voluntary striated muscles of the oropharynx
- It is completed by the involuntary contraction of the smooth muscle of the esophagus in a coordinated sequence

2- **Dysfunction** at either step can cause dysphagia

3- **Achalasia**

- Motility disorder of the esophagus characterized by failure of relaxation of the lower esophageal sphincter with aperistalsis in the body of the esophagus (atony)

4- **DES**

- Characterized by high amplitude simultaneous contractions in the smooth portion of the esophageal body (hypermotility)

5- **Nutcracker esophagus (super squeezer)**
  - Characterized by normal LES function and motility, however the contractile amplitude is usually 2-3 times the normal value and most patients also have an abnormal prolongation of the peristaltic wave

Etiology

1- **Striated muscle dysfunction**
  - Cerebrovascular accident
  - Myasthenia gravis
  - Polymyositis
  - Parkinson's disease
  - Amyotrophic lateral sclerosis

2- **Smooth muscle failure**
  - Invasive cancer
  - Infectious (Chagas' disease)
  - Neurologic
    - Achalasia
    - Diffuse esophageal spasm
    - Nutcracker esophagus
  - Autoimmune (scleroderma)

Pathophysiology

1- **In striated muscle**
  - Neuromuscular dysregulation results in the loss of a coordinated swallow and can lead to oropharyngeal dysphagia, regurgitation and pulmonary aspiration

2- **Smooth muscle dysfunction**
  - Caused by the loss of inhibitory neurons in the esophagus leading to disorganized peristalsis (mainly in the form of loss of sequencing of peristalsis, simultaneous waves, exaggerated wave amplitude and

prolonged wave duration) and increased LES tone with abnormal sphincter relaxation during swallows

Clinical features

1- **The most common symptoms of esophageal motor disorders are**
  - Dysphagia
  - Chest pain

2- **The most common symptoms of oropharyngeal dysphagia are**
  - Drooling
  - Regurgitation of food immediately after swallowing
  - Pulmonary aspiration

3- **Patients with diffuse esophageal spasm or nutcracker esophague**
  - Often present with intermittent retrosternal chest pain exacerbated by hot or cold items
  - Chest pain sometimes radiates to other parts of the body however , it is important to rule out myocardial ischemia

4- **Features of achalasia**
  - More common in middle aged females
  - Intermittent dysphagia to fluids and to solid foods
  - Retrosternal chest pain occurs with vigorous non peristaltic contraction of the esophagus
  - Putrefaction of the retained food leads to halitosis
  - Chest infections may occur due to aspiration during sleep
  - Weight loss is usually not marked

5- **A description of regurgitated contents** is useful in differentiating esophageal versus oropharyngeal causes

6- **A history of travel** to central and south America my warrant workup for Chagas' disease

7- **The history should focuse** on conditions that can cause motility disorders as
  - Cerebrovascular accident
  - Amyotrophic lateral sclerosis
  - Myasthenia gravis

8- **Physical examination should include**

  - Thorough neurologic examination
  - Assessment of nutritional status

Investigations

1- **Barium swallow**

  - Achalasia
    - Characteristic "bird's beak" tapered distal esophagus with proximal dilatation
    - This appearance can also occur with neoplastic compression of the lower esophagus (pseudoachalsia)
  - Diffuse esophageal spasm
    - Typical "corkscrew" or " rosary bead" appearance
  - Nutcracker esophagus
    - Often appears normal on barium swallow

2- **High resolution manometry**

  - Achalasia
    - Lack of primary peristalsis and increased LES tone (failure to relax)
    - If patients have simultaneous and repetitive contractions, the disease is termed " vigorous achalasia"
    - There are 3 identified types [all forms are associated with elevated LES postswallow residual pressures]

      © Type 1: low amplitude esophageal body pressure compartmentalization reflecting esophageal dilation

      © Type 2: high amplitude pressure compartmentalization

      © Type 3: spastic features in ≥ 20% sequences
  - Diffuse esophageal spasm
    - > 20% simultaneous contractions involving the smooth muscle esophagus
  - Nutcracker esophagus

        - Defined by elevated distal esophageal peristaltic amplitude > 180 mmHg

3- EGD

- In suspected cases of achalasia, EGD should always be performed to exclude mass lesions as a cause of pseudoachalasia
- In achalasia, the endoscope can pass easily through the narrowing without resistance
- EGD is typically normal in patients with DES or nutcracker esophagus

4- Chest X-ray

- In achalasia, showing absence of gases in the fundus of the stomach

Treatment

1- Medications

- Achalasia
    - Endoscopic botulinum toxin injection of the LES may temporize symptoms till more effective therapy is available
    - Can be used as sole therapy in elderly patients where more effective modalities are contraindicated because of comorbidities (calcium channel blockers can also be tried in elderly)
    - Effective therapy requires repeated injection, as efficacy wanes after a median of 9-12 months
- DES and nutcracker esophagus
    - Can be treated with nitrates and calcium channel blockers for symptomatic relief
- Spastic disorders
    - Have a perceptive component to symptomatology, presumably from coexistent visceral hypersensitivity that may require neuromodulator therapy (e.g. low dose tricyclic antidepressants particularly for chest pain)
- Obstructive symptoms (dysphagia, regurgitation)
    - May improve with botulinium toxin injection if abnormal LES relaxation can be demonstrated

- If acid reflux contribute to symptoms
    - PPIs therapy is given
- Scleroderma
    - Aggressive acid control with high dose PPIs

2- Other nonpharmacologic therapies

- Achalasia
    - Endoscopic pneumatic dilation of the LES to 30-40 mm disrupts the LES and is effective (often offering immediate relief)
    - Esophageal perforation can occur in 2-5% and may require emergency surgery
- DES and nutcracker esophagus
    - Endoscopic dilation is typically not useful

3- Surgical management

- Achalasia
    - (Heller's operation) Laparoscopic surgical myotomy of the LES (i.e. division of the muscle at the lower end of the esophagus) with partial fundoplication may offer definitive resolution of achalasia symptoms with the added benefit of protection against reflux with the fundoplication
    - The choice between surgical myotomy and pneumatic dilation depends on institutional expertise

4- Follow up

- Patients with achalasia have an increased risk of squamous cell esophageal carcinoma (2-7%) and there is debate whether regular surveillance EGD should be performed

Globus

1. **Definition:**
   - Persistent or intermittent sensation of a lump or foreign body in the throat
   - This sensation is present between meals
   - No dysphagia on swallowing
2. **Cause**
   - Probably a functional disease
3. **Treatment**
   - Reassurance
   - Antireflux therapy

Hiatus hernia

Sliding hiatus hernia

Definition

1. Herniation of the **gastro-esophageal junction** through the esophageal hiatus in the diaphragm into the thorax
2. This will affect the valvular mechanism of the gastro-esophageal junction leading to **reflux** of gastric contents into the esophagus

Clinical features

1. **Heart burn (pyrosis):**
   - It is a burning retrosternal pain occurring in lying down or leaning forward, and is severe during sleep
2. **Dysphagia**
   - May occur due to esophageal stricture
3. **Bleeding**
   - Due to esophagitis (hematemisis, melena or iron deficiency anemia)
4. **May be asymptomatic**

Investigations

1- Barium swallow
2- Upper endoscopy

Treatment

1- Medical therapy
  - Weight reduction
  - Small meals
  - Sleeping in semi-sitting position
  - PPIs and H2 blockers
  - Prokinetic drugs e.g. domperidone

2- Surgery
  - Fundoplication indicated in resistant cases

Para-esophageal or rolling hernia

Definition

1- A small part of the **fundus of the stomach** rolls up alongside the esophagus through the hiatus

Clinical features

1- **No reflux symptoms** ; as the gastro-esophageal junction remains in normal position
2- May lead to **mediastinal syndrome** if severe
3- Gastric volvulus or strangulation may occur

Treatment: surgery indicated in severe cases

GASTRIC DISORDERS

H.pylori infection

Definition

1- It is a microaerophilic, flagellated, highly motile, gram-negative, urease producing spiral bacteria that was first isolated from mucosal biopsies of patients with chronic active gastritis

2- It colonizes the mucous layer in the gastric antrum but is found in the duodenum only in areas of gastric metaplasia

3- It is protected from gastric acid by the juxtamucosal mucous layer (found under it) which retains bicarbonate secreted by antral cells, and ammonia produced by bacterial urease

Pathogenesis

1- Age: primarily during childhood and usually persists for life unless the infection is adequately treated.

2- Incidence: 30-60% of western populations are affected with higher prevalence in underdeveloped countries (80-90%)

3- The major risk factor for infection is the socioeconomic status of the family during childhood.

4- HP has been found in water, stool, dental plaque, and saliva.

5- Mode of transmission: faecal–oral or oral–oral, either by kissing or ingestion of food or water contaminated with the organism

6- Consequences of infection (important part)

- Neutrophilic gastritis
- Chronic active gastritis
- Atrophic gastritis and ↓ vitamin B12
  - Gastritis may be confined mostly to the gastric antrum and/or involve the entire stomach

    - Once patients develop severe atrophy, intestinal HP metaplasia or gastric adenocarcinoma may not be present in these tissues where there is no acid secretion
- Peptic ulcer disease
- Gastric intestinal metaplasia
- Gastric adenocarcinoma
- lymphocytic infiltration of gastric mucosa with lymphocytic follicle
- Gastric mucosa-associated lymphoid tissue (MALT) lymphoma
    - Regress after HP eradication
- Gastric B-cell lymphoma
    - Not regress after HP eradication
- Interestingly, in persons treated with PPIs chronically, there is usually a shift of HP infection from the antrum to the corpus and accelerated atrophic changes. Thus some experts advise eradication of HP before long-term PPI therapy is instituted in HP-infected individuals.
- GERD and HP:
    - No evidence that H. pylori causes GERD, however it may be protective or reduce its severity
    - Some patients who have no reflux symptoms of the disease may develop GERD once treated with eradication regimen.
- HP associations
    - Ischemic heart disease; it's theorized that high levels of cytokines induced by H. pylori leads to increased systemic inflammatory response & atherosclerosis.
    - Idiopathic chronic urticaria, alopecia areata & acne rosacea
    - Raynaud phenomenon & migraine headache have been observed to improve with H. pylori eradication.
    - Idiopathic thrombocytopenic purpura & refractory iron deficiency anemia have also been linked to H. pylori infection & improved in some individuals with eradication therapy.

7- Virulence factors

- Motility
  - Spiral shape and unipolar flagella allow its movement from the gastric lumen with low pH to gastric mucosal surface where pH is neutral, as well as to other parts of the gastric surface where its growth potential is optimal.
- Adherence factors
  - HP binds to gastric mucosal cell receptors (Lewis antigen) by several adhesion proteins (as BabA adhesion)
  - This tissue tropism and binding prevents the organism from being easily shed during cell and mucus turnover.
  - Ulcers are commonest when the infecting strain expresses CagA (cytotoxic-associated protein) and VacA (vacuolating toxin) genes
- Urease
  - HP produces urease, an enzyme which hydrolyzes urea to produce ammonia (NH_3) to protect itself from gastric acid.
  - Ammonia neutralizes the acid surrounding HP as well as provides an essential basis for the "CLO" test used for testing mucosal biopsies for the presence or absence of HP.
- Toxins
  - HP possesses and/or elaborates various toxins that cause tissue injury of the gastric mucosa in infected individuals.
  - These include lipopolysaccharide (endotoxin bound to HP), neutrophil activating protein (NAPA), vacuolating cytotoxin (VacA), cytotoxin-associated antigen (CagA-A), and outer membrane inflammatory protein (OipA).
  - Not all strains of HP possess all these toxins. Those strains of HP which possess CagA and OipA seem to be exceptionally virulent and are associated with more severe disease activity, PUD, and cancer.

Diagnosis

1- Endoscopy and biopsy

- The gold standard for the diagnosis of HP.
- Site of biopsy → Biopsies should be obtained from all parts of the stomach since the colonization of HP is spotty
- Stain of HP → Giemsa stain
- Histology also detect :
    - Gastritis
    - Gastric atrophy
    - Intestinal metaplasia
    - MALT lymphoma and cancer.
- Sensitivity ranges from 90% - 95% and specificity 95% - 100%.
- False negative results occur with:
    - Recent GI bleeding
    - Use of Bismuth-containing medications
    - Antibiotics
    - Sucralfate
    - Acid-suppressive medications.
- CLO test, PyloriTek test uses a biopsy in a medium containing urea which undergoes color change if HP is present with urease activity as ammonia ↑ the PH of the solution
- Culture of HP from gastric biopsies
    - Considered in patients who have failed 2 courses of appropriate antibiotic treatment regimens (resistant HP).

2- Breath tests

- Ingesting C_{14} (radioactive) or C_{13} containing urea, then blowing into a container to measure the tagged CO_2 released by HP degradation of urea ($CONH_3$) by its urease which releases CO_2 and NH_3.
- Sensitivity 85% - 95% and is operator-dependent.
- False negative results occur with history of recent :
    - Antibiotic
    - Bismuth, sucralfate

- Antisecretionary therapy
- Or atrophy and intestinal metaplasia.

3- **Stool antigen test**

- Has a similar sensitivity and specificity to breath tests.
- Useful for diagnosis and follow up
- False negative tests are seen as in breath tests as well as in patients with a history of recent GI bleeding.
- Both the breath test and stool antigen test should not be done for at least 4 weeks after HP eradication therapy.

4- **Serology**

- IgG HP antibody → may be +ve but lack sensitivity and specificity
- IgG HP antibody may persists even after proper eradication (at least for 18 months) and thus it is not a good measure of current infection

5- **Indications of HP testing**

- HP testing is recommended for patients who are to be treated for the eradication of HP infection.
- In patients with history of PUD and dyspepsia, if endoscopy is indicated, biopsies should be obtained from multiple sites.
- In patients with gastric ulcer, biopsies should also be obtained from the ulcer to check for cancer.
- After eradication therapy, testing for presence of HP is not routinely practiced.
- In patients with PUD-related GI hemorrhage or those with recurrent dyspeptic, symptoms may be tested for HP after at least 4 weeks have elapsed from eradication, antibiotic, and acid antisecretory therapy. Stool antigen test, breath test and, in indicated cases, endoscopy and biopsy may be used.

Treatment

1- **Combination therapy** is required for successful HP eradication.

2- **Triple-therapy** is based upon a PPIs taken with 2 antibiotics (clarithromycin & amoxicillin or metronidazole) For 10-14 days. Success is achieved in 90% of patients.

3- **Second-line therapy** should be offered to those who remain infected after initial therapy once reasons for failure of first-line therapy have been established.

4- **Quadruple-therapy** should be offered for those who remain infected after two triple therapies.

5- **Indications for HP eradication (if +ve tests)**

- Patients with past or active ulcer disease.
- Patients with low-grade MALT lymphoma as eradication may result in cure of the lymphoma.
- Patients at high risk of gastric cancer (e.g. +ve family history).
- Older patients on NSAIDs therapy.

6- **Treatment regimens**

- Triple therapy:
  - First-line therapy: the standard triple therapy 10-14 days.
  - PPI (e.g. Omeprazole 20 mg or lansoprazole 30 mg) twice/day.
  - Clarithromycin 500 mg twice/day
  - Amoxicillin 1 gm or metronidazole 500 mg twice/day
  - Metronidazole substitution should be used only for penicillin-allergic individuals due to high prevalence of metronidazole-resistant organisms
  - Second-line therapy: 10- day sequential therapy
  - PPIs & amoxicillin (1 gm), each administered twice/day for 5 days.
  - PPIs, clarithromycin (500 mg) & tinidazole (500 mg), all administered twice/day for another 5 days.

- Quadruple therapy: 14 days
  - PPIs twice/day.
  - Tetracycline (500 mg) 4 times/day.

- Metronidazole (500 mg) 4 times/day.
- Bismuth (2 tablets) 4 times/day

7- Causes of treatment failure

- Patient noncompliance
- Smoking
- Concurrent use of sucralfate
- Bacterial resistance to antibiotics.

8- In patients who are allergic or wish another regimen (10 day course of)

- levofloxacin 500 mg q.d. or 250 mg b.i.d., amoxicillin 1g b.i.d. and a PPI b.i.d. or
- Rifabutin 300 mg q.d., amoxicillin 1 g b.i.d. and a PPI b.i.d. may be used

9- Side effects of H.pylori eradication

- Diarrhea (clostridium difficile-associated colitis may occur).
- Ambdominal cramps, nauaea, vomiting.
- Rash.
- Flushing, vomiting when taken with alcohol (metronidazole).
- Headache.
- Rifabutin may cause bone marrow suppression, leukopenia, hepatitis, uveitis, and a polyarthralgia-like syndrome

Follow up

1- **Urea breath test & stool antigen test** are appropriate for follow-up
2- Both tests should be done **4 weeks after** eradication therapy
3- The annual recurrence rate after eradication is 5% in developing & < 1% in developed countries

Acute gastritis

Definition

1- Acute superficial inflammation of gastric mucosa

2- Sometimes associated with multiple small mucosal erosions (erosive gastritis)

3- Acute gastric ulcers occurs in the same setting as erosions but ulcers are larger

Causes

1- Irritant agents

- Aspirin and NSAIDs
- Corticosteroids
- Chemotherapy
- Macrolides
- Potassium and iron preparations
- Alcohol and smoking

2- Stress ulcers → usually in ICU patients

- Usually in the setting of severe or often multisystem illness
- Patients in a medical ICU esp. those who require respirators
    - Hemorrhage, shock, burns, MI, head trauma or stroke (cushing ulcer)
- Elderly patients in a surgical ICU with heart and lung disease

3- Curling ulcer → 2ry to burns

4- Bacterial infection→ H.pylori (initial infection)

5- Viral infection→ CMV and HSV in immunocompromised patients

6- Bile reflux following gastric surgery

7- Accidental ingestion of **caustic substances** such as strong alkali

Clinical picture

1- Epigastric pain and tenderness

2- Nausea and vomiting

3- Anorexia and dyspepsia

4- Belching either does not relieve the pain or relieves it only briefly

5- Hematemeis and melena

6- Anemia (chronic blood loss)

7- May be asymptomatic and abruptly presented by hematemesis

8- Complications include: chronicity, perforation or bleeding

Investigations

1- **Upper endoscopy**
   - Diffuse mucosal hyperemia and edema with multiple small superficial erosions and ulcers
   - Stress ulcers
     - Site → any where within the stomach and proximal duodenum, but more likely to occure in fundic mucosa (ordinary peptic ulcers typically found in the gastric antrum and the duodenum)
     - Characters → ulcerations may be superficial and confined to the mucosa (erosions) ± causing diffuse mucosal oozing of blood **or** may penetrate deeper into the submucosa which may erode into a submucosal vessel causing frank hemorrhage
     - No → may be one but often multiple ulcers
2- **Biopsy needed to exclude PUD or malignancy**
   - Epithelial injury and denudation and variable necrosis of the superficial glands.
   - Hemorrhage in to the lamina propria may be seen.
   - Inflammatory cells are not present in large numbers, though, the neutrophils are the predominant

Treatment

1- **Indications for prophylaxis treatment**
   - Patients on NSAIDs
   - ICU patients esp.
     - Those who are on respirators and have multisystem disorder
     - Those with history of peptic ulcer or upper GIT bleeding
2- **Drugs used for prophylaxis:**
   - I.V. PPIs → the most appropriate therapy (keep intragastric PH > 5)
   - Or I.V. ranitidine
3- **Specific treatment**
   - Treat the cause
   - Stop NSAIDs or other irritants

- Short term symptomatic therapy with antacids and acid suppression with proton pump inhibitors or antiemetics may be necessary
- Stress ulcers
  - Gastric wash by cold saline and antacids by ryle tube
  - I.V PPIs or rantitidine
  - Misoprostol (100-200 µg 4 time/day)

Chronic gastritis

Definition

1- Inflammation of the lining of the stomach that occurs gradually and persists for a prolonged time
2- Can lead to mucosal atrophy including loss of parietal and chief cells with subsequent metaplasia

Causes

1- Autoimmune (type A) → leading to pernicious anaemia
2- Bacterial (type B) → H.pylori infection
3- Chemical → biliary reflux (post pastrectomy)
4- Chronic abuse of NSAIDs or aspirin
5- Eosinophilic gastritis
6- Lymphocytic gastritis
7- Idiopathic e.g. granulomatous gastritis
8- Menetrier disease
9- Degeneration of the stomach lining from age

Clinical picture

1- Most patients are asymptomatic.
2- Some patients may present with mild epigastric discomfort, pain, nausea and anorexia
3- Patients with autoimmune gastritis have pernicious anemia and may have evidence of other organ specific autoimmunity esp. thyroid disease
4- May be complicated by gastric carcinoma

Investigations

1. **Upper endoscopy with biopsy**
    - No features or loss of normal rugal folds
    - Increased lymphocytes and plasma cells in the mucosa around the parietal cells.
    - Neutrophils are rare.
    - Mucosa may show changes of intestinal metaplasia.
    - At the end stage, mucosa is atrophied with absent parietal cells.
    - In H.Pylori infection, the organism may be noted
2. **Parietal cell antibodies and intrinsic factor antibodies** in autoimmune gastritis

Treatment

1. Treatment of the cause
2. Endoscopic screening for gastric carcinoma
3. No treatment required in most patients (asymptomatic)
4. Patients with dyspepsia may be benefited from H. pylori eradication.

Difference between acute gastritis and chronic gastritis

1. Acute gastritis is often erosive and hemorrhagic but chronic gastritis is not
2. NSADs and alcohol are the common causes of acute gastritis while autoimmunity and H Pylori are the common causes of chronic gastritis
3. Endoscopically inflammatory changes are seen only in acute gastritis
4. Neutrophils are the predominant inflammatory cell in acute gastritis while lympho-plasmatic infiltration is seen in chronic gastritis
5. Chronic gastritis has an increased risk of gastric carcinoma, especially type A, which is considered as pre malignant

Gastric diseases causing anemia

1. Peptic ulcer → microcytic anemia
2. Chronic gastritis → megaloplastic anemia
3. Gastric carcinoma → microcytic anemia
4. Gastric bypass or gastrectomy → microcytic anemia

Gastric carcinoma

Gastric adenocarcinoma

> 90% of cases

Pathogenesis

1- **Pathology**

- Early gastric cancer (EGC):
  - Not penetrated the major muscle layer of the stomach wall.
  - Divided into 3 types based on macroscopic appearance

    © Type i → protruded

    © Type ii a → superficially elevated

    © Type ii b → superficially flat

    © Type ii c → superficially depressed

    © Type iii → excavated

    © Combined types (ii c and iii)
- Advanced gastric cancer:
  - Penetrated the muscle layer of the stomach.
  - Divided into 3 types:

    © Polypoid or intestinal (cauliflower mass)

    © Diffuse infiltrating or signet ring type

    © Ulcerating

2- **Risk factors**

- Chronic atrophic gastritis with H.pylori infection
  - Causing gastric intestinal metaplasia → adenocarcinoma
  - CagA+ strains appear to be more carcinogenic than CagA- strains
- Achlorhydria
  - Pernicious anemia
  - Atrophic gastritis
- Gastric adenomatous polyps
- Atrophic changes e.g. atrophic gastritis, intestinal metaplasia
- Hypertrophic gastropathy (Menetrier's disease)

- Postgastrectomy
- Diet e.g. high salt consumption,spicy food, dietary nitrates, smoking or spirits
- National origin e.g. high risk in Japan, Chile, Finland
- Males vs. female (1.5: 1) , age > 45yr
- Blood group A
- Diet rich in fresh fruits and vegetables, daily aspirin use, and COX-II antagonist reduce the risk

Clinical presentation

Early gastric cancer

1- Typically asymptomatic
2- Usually discovered during endoscopy performed for other complaints.
3- Vague symptoms (epigastric discomfort and nausea)

Advanced gastric cancer

1- Most patients have advanced disease at the time of presentation

2- **Symptoms:**

- Abdominal pain and weight loss (epigastric pain not differentiated from the pain of PUD)
- May be accompanied by signs of gastric obstruction, such as early satiety or vomiting
- Anorexia, weakness may be present
- Gross hematemesis is unusal, but anemia from occult blood loss is frequent
- Dysphagia in tumors involving the fundus

3- **Physical examination**

- An epigastric mass
- An enlarged liver or ascites due to metastases
- An umilical mass is unusal (Sister Joseph's nodule)
- Metastasis to the ovaries (Krukenberg's tumor)
- Hard lymph node in the left supraclavicular fossa (Virchow's node)
- Paraneoplastic syndromes with cancer stomach:

  - Trousseau's syndrome (thrombosis)
  - Membranous nephropathy
  - Acanthosis nigricans
  - Seborrheic keratosis (Laser-Trelat sign)
  - Dermatomyositis

Investigations

1- **Upper GI x-ray series (barium meal) :**

- Findings:
  - Mass lesion (irregular filling defect)
  - Ulceration
  - Irregularity of the mucosa
  - lack of distensibility of the stomach
  - Linitis plastic (infiltration throughout the entire stomach)
  - Or no definite abnormality.
- Any of these findings requires endoscopic confirmation and biopsy

2- **Endoscopy and biopsy**

- In ulcerating lesions, 6 - 8 biopsies of the ulcer edges are necessary to provide a 95% chance of obtaining a positive result
- An acid pH of the gastric aspirate indicates, of course, that the stomach is capable of secreting acid.
- On the other hand, a neutral pH at endoscopy does not necessarily indicate achlorhydria.

3- **Endoscopic ultrasound**

- Determine the depth of invasion of the tumor(excellent for staging of gastric cancers)
- Allow accurate diagnosis of EGC which may be treated by endoscopic mucosal resection (EMR).

4- **Serum carcinoembryonic antigen (CEA) levels:**

- ↑ in about 1/3 of patients with advanced gastric cancer but are not helpful in making the diagnosis.

- Serial CEA useful in the postoperative follow-up of patients to indicate recurrences or to estimate metastatic tumor burden.

5- **↑ alkaline phosphatase level**

- May indicate metastases to the liver.
- ↑ 5′-nucleotidase level confirms that the liver is the origin of the abnormality in alkaline phosphatase.

6- **CT scan of the abdomen:** → detect liver metastases, lymph node enlargement, and the extent of the primary tumor.

7- **If endoscopic biopsy fails to make a histologic diagnosis:**

- CT- or ultrasound-guided needle aspiration of a mass lesion
- Or a percutaneous liver biopsy in patients with elevated alkaline phosphatase may provide diagnostic tissue.

8- **CBC**

- Typically microcytic anemia but Hb and Ht may be normal
- If pernicious anemia is the risk factor → macrocytic anemia

Treatment

1- **Surgery**

- Operable:
  - Radical and total gastrectomy with extensive lymph node dissection and lymphadenectomy
  - + esophago-jejunostomy
  - + post operative chemotherapy plus radiation
- Inoperable:
  - Pyloric obstruction → palliative gastro-jejunostomy
  - Cardiac obstruction → Celestin tube
  - Laser ablation
  - Celiac plexus block, narcotics
- Results of surgery:
  - 20% of patients are inoperable because of the extent of disease or high operative risk.

  - Of the remaining 80% who undergo surgery, about half undergo a curative resection, and the other half are given palliative treatment for bleeding or obstruction.
  - However, only about 20% of patients who have had a curative resection survive 5 years.
  - Results might be better with extensive lymph node dissection and lymphadenectomy.

2- **Chemotherapy and radiotherapy**

- If the patient's condition is operable, the initial resection of as much tumor mass as possible seems to improve the efficacy of chemotherapy and radiotherapy.
- Adjuvant chemotherapy using 5-fluororacil, mitomycin, doxorubicin, Cisplatin, and irinotecan seems to improve survival.
- Adjuvant radiotherapy alone has no effect on long-term survival.

3- **Other treatment measures**

- Careful attention to nutritional needs.
- Partial or complete gastric resection imposes additional nutritional consequences
- Supplemental vitamins, particularly vitamin B_{12}, and minerals such as calcium and iron.

4- **Follow up of operable cases**

- Clinical evaluation:
  - Every several months
  - Weight loss, gastrointestinal bleeding, and obstruction—all the signs of original disease—may signify recurrence.
- Investigations:
  - CBC, routine liver tests, and CEA level every 3 - 6 months for the first 1 - 2 years after surgery and every 6 - 12 months thereafter.
  - Yearly upper GI endoscopy to look for local recurrence during the first 5 years.

Prognosis

1- Generally poor.
2- The overall 5-year survival rate is 18.6%.
3- Untreated, the median life expectancy in advanced disease with liver metastases is 4-6 months and in patients with peritoneal carcinomatosis 4-6 weeks.
4- However, if the tumor is confined to the mucosa and submucosa (EGC) and there are no metastases or lymph node involvement, the 5-year survival rate exceeds 90%.

Gastric lymphoma [® the same risk factors, clinical picture and investigations]

Origin

1- 1ry gastric lymphomas → most of the noncarcinomatous gastric malignancies
2- 2ry by disseminated lymphoma or by metastatic cancer from other sites
3- MALT lymphoma

Treatment

1- If the lymphoma is confined to the stomach → surgical treatment ®
2- If regional nodes or distant sites are involved → radiotherapy or chemotherapy ± surgery

Prognosis

1- Because lymphoma responds better than adenocarcinoma to radiation and chemotherapy, the prognosis is better.
2- The 5-year survival rate of patients with gastric lymphoma is about 50%.

MALT lymphoma

1- Origin and etiology:

- Low-grade B-cell lymphomas of mucosa-associated lymphoid tissue (MALT) are thought to arise within organized lymphoid tissue in the gastric mucosa
- Most frequently acquired in response to H. pylori infection.

2- Treatment

- low-grade MALT lymphomas
    - Long-term remissions can be induced 70% - 80% of cases by the successful eradication of the H. pylori infection ®.

  - The lymphomas that are most likely to respond to the H. pylori eradication are those that are located superficially within the gastric mucosa.
  - Recurrences of low-grade lymphoma are encountered in patients treated by H. pylori eradication, but these appear to be infrequent and may be self-limiting and spontaneously regress without surgery.
- Deeper and higher grade lesions:
  - Treate as B-cell lymphomas

SMALL BOWEL DISORDERS

Intestinal tuberculosis

Site

1- **The commonest site** : ileocecal region, but any region of the gut may be affecting starting from the esophagus down to the anal canal

2- **Less common sites** : colon, appendix and jejunum

3- **The ileocecal region** is characterized by a maximal lymphoid tissue and a relative stasis of the chyme which favours infection

Infection types

1- Primary or bovine type

- It indicates intestinal TB without extraintestinal lesions
- Mode of infection → ingestion of contaminated milk obtained from an infected cow
- The causative organism → Mycobacterium bovis

2- Secondary or human type

- It is associated with pulmonary TB
- Mode of infection → ingestion of infected sputum from an open lung lesion
- Causative organism → Mycobacterium tuberculosis (human type)

Pathological types

1- Ulcerative type

- Infection starts in the submucosa with granuloma formation that gradually extends inwards to the mucosa causing mucosal ulcerations and outwards to the muscularis causing moderate induration of the wall
- Ulcers are characteristically circumferential with irregular edges and shaggy or nodular floors
- The lesions occur in short segments with intervening skip areas
- They differ from Crohn's disease in the shape of the ulcers and shortness of the affected segments
- Mesenteric lymphadenitis is common and often reveals typical caseating granulomas

2- Hyperplastic type

- It occurs in the presence of high immunity of the host or low virulence of the organism
- It causes fibrosis more than ulceration
- The intestine and the mesentery are greatly thickened and matted together by adhesions forming masses
- The mucosa shows polypoid masses with frequent strictures, these masses may be radiologically indistinguishable from cancer
- When perforation occurs → leads to a confined abscess rather than to free peritonitis
- Mesenteric lymphadenitis is common and more informative about the nature of the disease than the intestinal lesion

Clinical presentations

1- Medical cases

- Primary type
    - Diagnosis is difficult as abdominal symptoms are non-specific
    - The diagnosis should be suspected in any case of chronic lower gut symptoms as diarrhea or pain in a patient who is malnourished, underweight and has a high ESR
    - The diarrhea is semi-liquid or watery and varies from 3-6 motions/day [steatorrhea may occur due to 2ry malabsorption]
    - The pain is commonly in the periumblical region or the right iliac fossa and is often ↑ by meals to the extent of sitophobia
    - Other symptoms include anorexia, progressive weight loss and prolonged fever
    - Even after barium follow-through and complete colonoscopy with ileal intubation and biopsy, the diagnosis may still remain in doubt → antituberculous drug regimen for 1 month is allowed as a therapeutic test
- Secondary type
    - Diagnosis not difficult due to associated pulmonary TB

- The diagnosis should be suspected in any patient with active pulmonary TB and complaining of chronic or recurrent lower abdominal symptoms
- Symptoms as in the primary group
- If barium follow through and colonoscopy don't establish the diagnosis → a full course of antituberculous drugs is given as it is the treatment for both the pulmonary and the intestinal lesions

2- **Surgical cases**

- Complicated cases
  - The patient may present by intestinal obstruction, perforation, bleeding, fistula or a palpable mass of unproven nature
  - Diagnosis only made by histological and bacteriological examination of the excised tissue
  - After operation → a full course of antituberculous drugs is given
- Appendicular cases
  - The patient may present by a picture like acute or chronic appendicitis for which appendicectomy is done
  - Diagnosis only made by histological and bacteriological examination of the removed appendix
  - After operation → a full course of antituberculous drugs is given [TB may be limited to the appendix or more commonly involves the ileocecal region as well]

Investigations

1- **Barium follow-through**

- The earliest changes → acceleration of the small intestinal motility and hypersegmentation and flocculation of barium
- Stierlin's sign → lack of barium retention in an inflamed segment with a normal column of barium on both sides
- String sign → persistent narrow stream of barium in the small intestine due to hypertonicity and stenosis [also seen in Crohn's disease]

- Fleishner's sign → triangular appearance of the terminal ileum with the base towards the cecum
- There may be evidence of masses, deformities or intestinal obstruction

2- **Colonoscopy**

- Complete colonoscopy to the cecum with intubation of the ileum is done
- Findings
  - Characteristic transverse or circumferential ulcers with skip regions will be seen in the cecum, terminal ileum and possibly also in the colon [in Crohn's disease the ulcers are mainly longitudinal or serpiginous]
  - The ileocecal valve is gaping and rigid [in Crohn's disease, it is closed and contracted]
  - Napkin deformities and polypoid masses may be seen
  - Biopsy → caseating or non-caseating granulomas, Z.N stain for acid fast bacilli and culture should be done

3- **Chest X-ray**

4- **Sputum examination**

5- **Tuberculin test**

Treatment

1- **Medical cases**

- In definitive diagnosis
  - Full course of antituberculous drugs is given for both primary and secondary cases ® → see TB
- In doubtful diagnosis
  - Primary type → short course of antituberculous drugs for 1 month as a therapeutic test
  - Secondary type → full course is given as the treatment is also applicable for the pulmonary lesion

2- **Surgical cases**

- Full course is given after the diagnosis is confirmed by histological and bacteriological examination of the excised tissues

Malabsorption syndrome

Definition

1- Failure to absorb or digest normally one or more dietary constituents

2- Most patients with malabsorption fail to absorb lipids leading to a syndrome characterized by large, loose, foul-smelling fatty stools and loss of weight. often carbohydrate, protein, and other nutrients also can't be absorbed.

Causes

1- **Pancreatic exocrine insufficiency**
  - Chronic pancreatitis
  - Pancreatic carcinoma
  - Cystic fibrosis

2- **Bile acid insufficiency**
  - Small bowel bacterial overgrowth
  - Crohn's disease of the terminal ileum
  - Severe parenchymal liver disease or cholestasis
  - Drugs [sequestration or precipitation of bile salts]
    - Neomycin
    - Calcium carbonate
    - Cholestyramine

3- **Small bowel mucosal disorders**
  - Celiac sprue
  - Tropical sprue
  - Collagenous sprue
  - Whippl's disease
  - Radiation enteritis
  - Ischemic disease
  - Intestinal lymphoma
  - Crohn's disease and TB

- Giardia lambilia infection
- Eosinophilic enteritis
- Amyloidosis

4- **Small bowel specific absorptive defects**

  - 1ry lactase deficiency
  - Abetalipoproteinemia

5- **Small bowel inadequate absorptive surface**

  - Short gut syndrome

6- **Lymphatic disorders**

  - Intestinal lymphangiectasia

7- **Mixed defects in absorption**

  - Zolliger – Ellison syndrome
  - Postgastrectomy disorders

8- **Endocrine disease**

  - DM
  - Hyperthyroidism and hypoparathyroidism
  - Adrenal insufficiency

9- **Cardiovascular disease** [congestion and hypoxia of intestinal mucosa]

  - Congestive heart failure and constrictive pericarditis

Clinical features

1- **Gastrointestinal manifestations [steatorrhoea]**

  - Weight loss and generalized malnutrition
  - The stools are: bulky, offensive, greasy and glistening
  - Chronic diarrhea : unabsorbed bile acids and fatty acids decrease absorption of water and electrolytes (↑ secretion)
  - Flatus and abdominal distension (fermentation of CHO)
  - Abdominal discomfort and pain
  - Steatorrhoea is severe in pancreatic insufficiency , mild to severe in mucosal diseases and mild to moderate in other causes

2- **Hematopoietic**

  - Anemia (# iron, folic acid and vitamin B12)

- Bleeding tendency (# vitamin K)

3- **Skin**

- Hyperkeratosis and dermatitis (# vitamin A)

4- **Nervous system**

- Peripheral neuropathy (# vitamin B12 and thiamine)
- Night blindness (# vitamin A)

5- **Musculoskeletal**

- Bone pain
  - Osteoporosis (# protein)
  - Osteomalacia (# Ca)
- Tetany and parathesia (# Ca)
- Weakness (# K and anemia)

6- **Genitourinary**

- Nocturia (delayed absorption of water)
- Azotemia and hypotension (fluid depletion)

7- **Manifestations of the cause ® e.g.**

- Celiac disease
- Tropical sprue
- Whipple's disease
- Crohn's disease

Investigations

1- **Blood tests**

- CBC
  - ↓ Hb and Ht → anemia
  - ↓ MCV → iron deficiency anemia
  - ↑ MCV → macrocytic normochromic anemia (B12 and folate)
- Liver function tests
  - Impaired overall function → presence of an organic disease
  - Impaired PT → malabsorption of fat-soluble vitamins (e.g. Vit K)
- Serum amylase
- Serum electrolytes

        - ↓ Ca, P, Na, K, Cl, magnesium
    - Serum proteins → ↓
    - Low cholesterol, TGs → fat malabsorption
    - Serum iron, folate , vitamin B12 → ↓

2- **Radiological studies**

- Plain X-ray , CT scan of the abdomen or ERCP: [not measure function directly- can detect]
    - Pancreatic calcification
    - Dilated or strictured pancreatic ducts
    - Pancreatic masses
- Barium meal and follow through study of small intestine
    - Malabsorption pattern
        - © Loss of the normal feathery appearance of jejunum
        - © Segmentation or clumping of barium
        - © The bowel may be dilated and the barium diluted because of increased intraluminal fluid
    - Crohn's disease → narrowed, irregular terminal ileum
    - Infiltrative process → thickening of the intestinal folds
        - © Lymphoma
        - © Whipple's disease
    - Diverticula, fistulas, and surgical alterations in bowel anatomy also may be evident

3- **Fecal fat determination**

- Qualitative screening test
    - Sudan stain for fecal fat → abnormally large or increased numbers (> 100/40 × field) of fat droplets suggest steatorrhoea
- Quantitative determination of stool fat (rarely performed nowadays)
    - More accurate than sudan stain but disagreeable (collecting stools over 72 hr)

        - Most normal people excrete up to 6 g of fat per 24 hours on a diet that contains 80 - 100 g of fat and avoiding of Mineral oil and oil-containing cathartics
        - In steatorrhoea → Stool fat > 6 g per 24 hours

4- Stool microscopy for protozoa like Giardia, ova, cyst and other infective agents

5- Serological tests e.g.

- IgA Anti-transglutaminase antibodies or IgA Anti-endomysial antibodies for Celiac disease

6- Pancreatic function tests

- Low fecal pancreatic elastase → indicative of pancreatic insufficiency
- Collection of pancreatic secretions, bicarbonate and enzymes from the duodenum:
    - After stimulation of the pancreas with secretin or with a test meal → HCO3 concentrations < 90 mmol/L suggest pancreatic insufficiency (unreliable)
- The bentiromide test (no duodenal intubation)
    - Administering a single oral dose of 500 mg of bentiromide after an overnight fast and the urine is then collected for 6 hours
    - Chymotrypsin cleaves the molecule within the lumen of the small intestine, releasing paraaminobenzoic acid (PABA) which excreted in the urine
    - < 60% excretion of PABA suggests pancreatic insufficiency
    - Not specific to pancreas (mucosal disorders, renal disease, severe liver disease, and diabetes also can cause low PABA excretion
- Glucose tolerance test → normal or diabetic in pancreatic malabsorption

7- Tests for bacterial overgrowth

- Bile acid breath test
    - Principle : conjugated bile acids resorbed with 95% efficiency in the terminal ileum
    - Patient is given radiolabeled [^{14}C]-glycocholate orally
    - Normally: 5% of it enters the colon and undergoes bacterial deconjugation

        - In bacterial overgrowth, bacteria promotes earlier bacterial deconjugation of [^{14}C]-glycocholate with release of large amount of ^{14}C- glycine which is metabolized and appears in the breath as $^{14}CO_2$
        - Similarly, disease or resection of the terminal ileum allows more bile acids to pass into the colon and undergo bacterial deconjugation, resulting in an increase in expired carbon dioxide
    - Enteroscopy for enteropathy and Culture of jejunal aspirate
        - Normally → $< 10^3$ organisms / ml
        - In bacterial overgrowth → $> 10^5$ organisms /ml
    - Low urinary and blood D-xylose levels
    - Low urinary excretion of cobalt-labeled vitamin B_{12}

8- Xylose tolerance test [the molecule remain intact after absorption]

- Screening test in diffuse small bowel mucosal disease
- We give 25 gm D-xylose orally and 5 hr urinary excretion is estimated with drinking 1 L of water during collection
- Normally → 5 hr urine should contain > 5 gm of xylose and the normal 2-hr blood xylose > 40mg/dl
- In small bowel mucosal disease, bacterial overgrowth → urinary and blood levels below normal
- The same results can occur in
    - Massive ascites
    - Renal failure and decreased circulatory volume

9- Tests for lactase deficiency

- Lactose tolerance test
    - The blood glucose level fails to rise > 20 mg/dL above the fasting level (flat curve)
- Breath hydrogen test
    - Excessive amounts of H2 absorbed and excreted by the lungs
- Stool acidity test
    - Reducing substances in stools

10- **Vitamin B12 absorption (Schilling) test**

- 24-hour urinary excretion of orally administered cobalt-labeled vitamin B_{12} is measured
- Normally, more than 10% of the labeled dose is excreted within 24 hours
- Significance :
  - Pernicious anemia or gastric atrophy
  - Pancreatic insufficiency (↓enzymes)
  - Terminal ileum mucosal diseases
  - Diphyllobothrium latum infection
  - Small-bowel bacterial overgrowth

11- **Upper endoscopy for Small-bowel biopsy (jejunal):** specific diagnosis of small bowel mucosal diseases

- Celiac sprue → subtotal villous atrophy
- Tropical sprue → partial villous atrophy
- Whipple's disease → macrophage infiltrating the villi
- Intestinal lymphangiectasia → dilated lymphatics within the cores of the villi
- Crohn's disease → ®
- Abetalipoproteinemia → villous epithelial cells are distended with fat

12- **Capsule endoscopy and colonoscopy** : occasionally useful

13- **Other investigations**

- Sugar probes or Cr^{51}-EDTA to determine intestinal permeability
- Se^{75}-HCAT test to diagnose bile acid malabsorption in ileal disease or primary bile acid diarrhea

Treatment

1- **Treatment of the cause ®**

- Surgery → for strictures or fistulas
- Antituberculous drugs → for TB enteritis
- Metronidazole → for giardiasis
- Antibiotics → for tropical sprue and whipple's disease
- Antibiotics and surgery → for stagnant loop syndrome

  - Gluten free diet → for celiac disease
  - Pancreatic enzyme supplements and analgesica → for chronic pancreatitis

2- Nutrients supplements

3- Total parenteral nutrition can be used

Celiac disease

Definition

1- It's immunologically mediated inflammation of small bowel resulting from intolerance to the protein gluten present in wheat and other similar proteins present in barley, rye & to lesser extent oat

Etiology

1- There is a 70% oncordance rate in identical twins and a prevalence of 10% in first-degree relatives.

2- HLA studies indicate that most celiacs possess DR3-DQ2 or DR5/7-DQ2 and some celiacs have DR-4-DQ8.

3- Patients with celiac sprue have inappropriate mucosal T-cell response to ingested gluten or prolamines from dietary grains resulting in intestinal mucosal injury.

4- The putative prolamines include gliadin in wheat, secalin in rye, and hordein in barley. Avenin in oats does not induce immunoreactivity.

5- It is thought that prolamines such as gliadin form an immunogenic complex with tissue transglutaminase (tTG). This gliadia-tTG complex forms the substrate for antigliadin antiendomysial and anti-tTG antibodies. The resulting T-cell response mediates small intestinal mucosal damage.

Clinical features

1- Age: peak incidence in adults in the 3rd and 4th decades

2- Sex: female > male

3- **Infancy** (usually at 6th month after introduction of cereals) and children presented with
    - Chronic diarrhea
    - Failure to thrive
    - Delayed pubertal growth in adolescents

4- **Classical presentation in adults:**
    - Malabsorption ®
    - Chronic Diarrhea
    - Bloating and flatulence
    - Weight loss.

5- **However, it can also present with:**
    - Anemia, chronic fatigue
    - Fibromyalgia
    - Short stature, infertility, seizures
    - Osteopenia and osteoporosis.

6- **It may coexist** with autoimmune and connective tissue disorders ®

7- **Patients with dermatitis herpetiformis**- blistering subepidermal eruption of the skin- (DH) often have the intestinal pathology; however, not all patients with CS have DH.

Conditions associated with celiac disease

1- **Anemia**
    - Iron deficiency
    - Folate deficiency
    - Vitamin B_{12} deficiency

2- **Neuropsychiatric disorders**
    - Peripheral neuropathy
    - Ataxia
    - Seizures
    - Cognitive deficits
    - Hyperactivity-attention deficit disorder

3- **Musculoskeletal disorders**

- Osteopenic bone disease
- Short stature
- Systemic lupus erythematosis
- Rheumatoid arthritis

4- **Endocrinal disorders**

- Type I diabetes mellitus (2-8%)
- Autoimmune thyroid disease (5%)
- Autoimmune adrenal disease

5- **Gastrointestinal disorders**

- Primary biliary cirrhosis (3%)
- Primary sclerosing cholangitis
- Autoimmune cholangitis
- Idiopathic hepatits and cirrhosis
- Lymphocytic gastritis
- Lymphocytic colitis

6- **Neoplastic**

- Non-Hodgkin's lymphoma
- Intestinal T-cell lymphoma
- Intestinal adenocarcinoma
- Oropharyngeal and esophageal squamous cell carcinoma

7- **Miscellaneous**

- Sjogren's syndrome (3%)
- IgA deficiency
- IgA nephrolpathy
- Infertility
- Prolonged prothrombin time

Complications

1- **Malignancy**

  - 2 -fold increased risk of enteropathy-associated T-cell lymphoma, small bowel carcinoma or squamous cell carcinoma of esophagus

2- **Ulcerative jejuno-ileitis**
  - Manifested by fever, abdominal pain, obstruction or perforation

Diagnosis [Confirmed with combination of clinical, serologic and histopathologic findings]

1- **Endomysial IgA antibody (EMA) and IgA tTG (tissue transglutaminase)**
  - Have 95% sensitivity and specificity, especially in classic cases of CS.
  - Both have lower sensitivity in patients with lesser degrees of villous atrophy and very young infants.

2- **IgA and IgG antigliadin antibodies (AGA)** are sensitive but nonspecific.

3- **Small-bowel biopsy** (jejuna or duodenal)
  - The golden standard test
  - At least 6 distal duodenal sites should be biopsied during endoscopy as the mucosal involvement may be patchy.
  - Biopsies should not be obtained from the duodenal bulb or the immediate post-bulbar duodenum since the presence of submucosal mucous glands in these areas may influence epithelial and mucosal histology.
  - Diagnostic features include:
    - Villous blunting (subtotal villous atrophy), the commonest cause
    - Deepening of crypts
    - Increased intraepithelial lymphocytes (IEL), monocytes, and plasma cells.
  - Other causes of villous atrophy should be considered
    - Tropical sprue
    - Whipple's disease
    - Zollinger-Ellison syndrome
    - Lymphoma
    - Radiation
    - Giardiasis
    - AIDS enteropathy

- Dermatitis herpitiformis
- Hypogammaglobulinemia

4- Serological tests **should not replace** small-intestinal biopsy findings for making the diagnosis of celiac sprue

- However, if small-intestinal biopsies are unavailable, the presence of high titer EMA or IgA tTG is most suggestive of CS.
- Because IgA deficiency is common in patients with celiac sprue (2.5%), IgA levels should be determined. In patients with IgA deficiency, IgG tTG may have value in diagnosing celiac sprue.

5- Other tests for malabsorption → see later ®

6- HLA-typing:

- HLA-DQ2 is positive in 90–95% of CD patients and HLA-DQ8 in about 8%, i.e. most of the rest. So, absence of both alleles has a high negative predictive value for celiac disease
- HLA typing is useful for ruling out the disease, for example in patients already on a gluten free diet

7- Hematology

- Folate deficiency is common, causing Macrocytosis & iron deficiency due to malabsorption of iron and increased loss of desquamated cells is common, so a blood film may show microcytes and macrocytes
- Features of hyposplenism may be found (hypersegmented polymorphonuclear leucocytes and Howell–Jolly bodies).

8- Biochemistry: in severe cases may reveal

- Biochemical evidence of osteomalacia (low calcium and high phosphate).
- Hypoalbuminemia

9- Radiology : small bowel follow – through show

- Dilatation of small bowel & slow transit
- Folds become thicker
- In severe cases total effacement may be seen
- Radiology is now mainly used when a complication (e.g. lymphoma) is suspected

10- **Bone densitometry (DXA)** should be performed on all patients because of the risk of osteoporosis

Treatment

1. **Gluten free diet** → rapid clinical and pathological improvement
    - The patient must avoid all wheat, barley, and rye. Rice, corn, soy, and the flours of these grains are acceptable.
    - Also avoid many commercially prepared foods, such as some brands of ice cream, some desserts, and meats that contain wheat fillers.
    - Even some vitamin and drug preparations are enclosed in capsules that contain small amounts of gluten, which may be sufficient to produce mucosal injury in some patients.
2. **Adjunctive treatment** of sprue may include folic acid, vitamin, calcium, and iron supplements
3. **Corticosteroids or immuno-suppressive drugs** may be needed in some cases to induce remission
4. **Follow up** [dietary adherence monitored by]
    - Serial Endomysial IgA antibody (EMA)
    - Serial IgA tTG

Tropical sprue

Definition

1. It's a **chronic progressive malabsorption** in residents or visitors to tropical areas, associated with abnormalities of small intestinal structure & function
2. The disease is **endemic in** most of Asia, some Caribbean islands, Puerto Rico and parts of South America

Pathophysiology

1. The epidemiological pattern & the occasional epidemic suggests that an infective agent may be involved
2. **No single bacterium** has been isolated, the condition often begins after acute diarrheal illness

3- **Small bowel bacterial overgrowth** with E. coli, Enterobacter & Klebsiella is frequently seen

4- The changes closely resemble those of celiac disease

Clinical features

1- Diarrhea, abdominal pain, fatigue

2- Anorexia, weight loss

3- **In visitor to tropics** severe diarrhea may be sudden, associated with fever occuring either a few days or many years after being in tropics

4- When the condition becomes **chronic**, features of folic acid malabsorption (megaloblastic anemia), other deficiencies (e.g. calcium, vitamin D) are common

5- **Remissions & relapses** may occur

Diagnosis

1- **Acute infective causes** of diarrhoea must be excluded particularly Giardia, which can produce a syndrome very similar to tropical sprue

2- **Malabsorption** should be demonstrated, particularly of fat and B12

3- **Biopsy**: partial villous atrophy.

Treatment

1- Severely ill patients require **resuscitation with fluids and electrolytes** for dehydration, and nutritional deficiencies should be corrected

2- **Folic acid (5 mg daily**); Many patients improve when they leave the sprue area and take folic acid

3- **Tetracycline** (250 mg 4 time/day for one month),may up to 6 months

4- **Vitamin B_{12}** (1000 µg) is also given to all acute cases

Prognosis

1- The prognosis is **excellent**

2- Mortality is usually associated with water and electrolyte depletion, particularly in epidemics

Whipple's disease

Definition

1- It's a rare condition affecting males, characterized by infiltration of small intestinal mucosa by **foamy macrophages** which stain positive with periodic acid-Schiff (PAS) reagent

2- The disease is **multisystemic** & almost any organ can be affected, sometimes long before GIT involvement becomes apparent

Pathophysiology

1- Infection with the gram +ve **Trophyrema whipplei** which is resident within macrophages in the bowel mucosa

2- **Villi** are widened & flattened

3- **Densely-packed macrophages** are found in the lamnia propria, that may obstruct lymphatic drainage causing fat malabsorption

Clinical features

1- Low-grade fever is common, arthritis precedes intestinal symptoms in most patients (often the first manifestataion)

2- Middle-age men are most commonly affected

3- Other presentation depends on the pattern of organ involvement:

GIT > 70%	Diarrhea (75%), steatorrhea, weight loss (90%), bloating, protein-losing enteropathy, ascites, hepatosplenomegaly (<5%).
Skeletal 65%	Seronegative large joint arthritis, sacroiliitis.
Hematological 60%	Anemia, lymphadenopathy.
Neurological 10-40%	Apathy, fits, dementia, myoclonus, meningitis, cranial nerve lesion.
Cardiac 10%	Pericarditis, myocarditis, endocarditis, coronary arteritis.
Pulmonary 10-20%	Chronic cough, pleurisy, pulmonary infiltrates.

Diagnosis

1- **Small bowel biopsy:** (investigation of choice).

  - Periodic acid–Schiff (PAS)-positive macrophages are present but nonspecific

    - On electron microscopy, the characteristic trilaminar cell wall of T. whipplei can be seen within macrophages and the macrophage infiltrating the villi
    - T. whipplei antibodies can be identified by immunohistochemistry
    - A confirmatory PCR-based assay is available
2. **Laboratory features of malabsorption** (e.g. macrocytic anemia, deficient vit K, D & deficient minerals Ca, phosphates & magnesium).

Treatment

1. **Ceftriaxone** 2gm daily IV for 2 weeks followed by **trimethoprim / sulphamethoxazole** double strength twice daily for 1 year
2. Or procaine penicillin G, 1.2 million units per day I.M or I.V. plus streptomycin 1g per day I.M. for 2 weeks followed by trimethoprim / sulphamethoxazole double strength twice daily for 1 year
3. Treatment periods < 1 year are associated with relapse in about 40%.
4. Ampicillin, tetracycline or chloramphenicol can be used

Small bowel bacterial overgrowth

Definition [blind-stagnant-loop syndrome]

1. It's a condition in which there is small intestinal bacterial overgrowth (i.e. 10^8-10^{10} organisms/mL), most of which are normally found in colon
2. While normally there is < 10^4 organisms/mL, derived from the saliva.

Causes

1. **Hypochlorhydria:**
    - Pernicious anemia
    - Long-term PPIs, H2 receptor antagonist
    - Partial gastrectomy
2. **Impaired intestinal motility**
    - Scleroderma
    - Diabetic autonomic neuropathy

- Hypothyroidism
- Chronic intestinal pseudo-obstruction

3- **Structural abnormalities (stasis):**

- Jejunal diverticulosis
- Stricture or enterocolic fistula (Crohn's disease).
- Extensive small bowel resection
- Billroth 11 gastrectomy with afferent loop stasis

4- **Impaired immune function**

- Hypogammaglobulinemia

Clinical features

1- Watery diarrhea &/or steatorrhea

2- Anemia due to B_{12} deficiency (probably due to uptake of vitamin B12 by microorganisms)

3- Symptoms of the underlying disease e.g. Crohn's

Investigations

1- **Barium follow-through:** may reveal blind loop or fistula

2- **Endoscopic small bowel biopsies: for**

- Exclusion of mucosal disease such as celiac disease
- Jejunal contents for bacteriological examination (i.e. aerobic & anaerobic culture techniques and bacterial count).

3- **Glucose hydrogen or C^{14}-glyocholic acid breath test** (non-invasive diagnosis):

- Breath samples are measured after ingestion of the test material
- Bacteria within the small bowel cause an early rise in breath hydrogen from glucose or C14 form C14-glyocholic acid.

4- **Investigations for hypogammaglobulinemia**

- Serum immunoglobulins are reduced.
- Intestinal biopsy shows reduced or absent plasma cells & nodules of lymphoid tissue (nodular lymphoid hyperplasia).

Treatment

1- **Specific:**

- Tetracycline 250 mg 4 times/day for 7 -10 days **or**

- Metronidazole 500 mg 3 times/day **or**
- Rifaximin 400 mg 3 times/day **or**
- Ciprofloxacin 250 mg twice/day

2- Symptomatic

- Treatment of the underlying cause: e.g. B12 injection for pernicious anemia and surgery for strictures and fistulas
- If bile acid deficiency not correctable → reduction of long chain triglycerides is indicated, give medium chain triglycerides (do not require bile acids for absorption)
- Antidiarrheal drugs (e.g. loperamide or diphenoxylate) in patients with motility disorders such as diabetes and sclroderma
- In hypogammaglobulinemia:
  - Control of giardiasis.
  - Immunoglobulin infusions.

Ileal resection

Characters

1- It's usually found after surgery of Crohn's disease

2- Vit B_{12} & bile salts malabsorption develops

3- Unabsorbed bile salts pass into colon stimulating water & electrolyte secretion resulting in diarrhea

4- If hepatic synthesis of bile salts can’t keep pace with fecal losses → fat malabsorption occurs

5- Another consequence is the formation of lithogenic bile leading to:

- Gall stones.
- Renal calculi rich in oxalates, as normally oxalates are bound to calcium but when bile salts reach colon they preferentially bound to calcium leaving oxalates free to be absorbed with subsequent formation of urinary oxalate stones.

Investigations

1- Test of bile acid absorption.
2- B12 deficiency → macrocytic anemia

Treatment

1- Cholestyramine: is a resin that binds bile salts in the intestinal lumen
2- Aluminum hydroxide is an alternative therapy
3- Parentral B12 supplementation is necessary

Short bowel syndrome

Definition

1- It's malabsorption resulting from extensive small bowel **resection or disease**
2- In adults it usually results from extensive surgery undertaken for **Crohn's** disease or **mesenteric infarction**

Types of patient

1- Jejunal resection with intact ileum & colon (uncommon and nutritional support is rarely needed).
2- Jejunum-colon patients (jejuno-ileal resection with jejuno-colic anastomosis).
3- Jejunostomy patients (jejuno-ileal resection & colectomy).

Pathophysiology

1- **Loss of surface area for digestion & absorption** are the key factor.
2- The process of digestion & absorption are usually completed within the first 100 cm of jejunum, so enteral feeding is usually possible if this 100 cm of small intestine remains.
3- **Normally**, the proximal small bowel reabsorbs most of 8 liters of fluids secreted daily, and patients with high jejunostomy are at high risk of hypovolemia, dehydration & electrolyte loss.
4- **The presence of part or all of the colon** may markedly improve these losses by increasing water reabsorption
5- **The presence of intact ileocecal valve** may ameliorate the clinical picture by slowing small intestinal transit & reducing bacterial overgrowth.

Clinical features

1. Severely affected patients have large volumes of jejunostomy fluid losses
2. If the colon is preserved, diarrhea & steatorrhea develops
3. Dehydration & signs of hypovolemia are common
4. Weight loss, loss of muscle bulk & malnutrition
5. Some patients are at satisfactory but precarious balance until a minor illness or GIT upset occurs when they rapidly become dehydrated

Treatment

1. **Immediately postoperative:**
    - Total parentral nutrition is started
    - PPI therapy is given to reduce gastric secretion
2. **Enteral feeding**
    - Cautiously introduced after 1-2 weeks under carful supervision and slowly increased as tolerated
3. **Long term management**
    - Monitoring of fluid & electrolyte balance
    - Adequate calorie & protein intake, fats are good energy source & should be taken as tolerated. Medium-chain triglyceride supplements are often given first because they are more easily absorbed
    - Use of oral/enteral rather than parentral nutrition whenever possible
    - Replacement of vitamin B_{12}, calcium, vitamin D, magnesium, zinc & folic acid
    - Antidiarrheal agents (e.g. loperamide or codeine sulphate)
    - Some patients are unable to maintain positive fluid balance, so octreotide (50-200 µg twice daily) reduces GIT secretions and is useful in such individuals

Radiation enteritis and proctocolitis

Definition

1- **Intestinal damage** occurs in 10-15% of patients undergoing radiotherapy for abdominal or pelvic malignancy
2- **The risk varies** with dose schedule & concomitant use of chemotherapy

Pathophysiology

1- Rectum, sigmoid colon & terminal ileum are most frequently affected
2- **Radiation causes** inflammation, edema, shortening of villi & crypt abscess formation. These eventually resolves completely except in some patients in whom obliterative endarteritis affecting endothelium of submucosal arterioles develops over 2-12 months.
3- Fibroblastic proliferation produces progressive ischemic fibrosis over years & may lead to adhesions, ulcerations, strictures, obstruction or fistula to adjacent organs

Clinical features

1- In acute phase:
   - Nausea, vomiting, abdominal pain & diarrhea
   - If colon & rectum are involved, rectal mucous bleeding & tenesmus occur

2- In chronic phase: develops over 5-10 years
   - Proctocolitis.
   - Bleeding from telangiectasia
   - Small bowel stricture
   - Fistula (e.g. rectovaginal, colovesical, enterocolic).
   - Adhesions → intestinal obstruction
   - Malabsorption: bacterial overgrowth, bile salts malabsorption

Investigations

1- Sigmiodoscopy: in acute phase shows changes resembles those of ulcerative proctitis
2- Colonoscopy: later to show the extent of lesion
3- Barium follow-through: shows small bowel strictures, ulcers & fistulas

Treatment

1- **Antidiarrheal drugs** (e.g. codeine phosphate, loperamide).
2- **Antibiotics** for ttt of bacterial overgrowth

3- **Cholestyramine** for bile salts malabsorption
4- **Corticosteroid** enema may help proctitis
5- **Endoscopic laser or argon plasma coagulation therapy** may reduce bleeding from proctitis
6- **Surgery** should be avoided as possible, because the injured intestine is difficult to resect & anastomose. However, it may be necessary in perforation, or fistula

Abetalipoproteinemia

Definition

1- It's a rare **autosomal recessive disorder** in which there is deficiency of apolipoprotein B resulting in failure of chylomicron formation, leading to fat malabsorption & deficiency of fat-soluble vitamins

Characters

1- **Jejunal biopsy** reveals enterocytes distended with resynthesized triglyceride with normal villous morphology
2- **Serum cholesterol & triglyceride** levels are low
3- **Other associated abnormalities** occur in this syndrome (e.g. acanthocytosis, retinitis pigmentosa, progressive neurological disorder with cerebellar & dorsal column signs)

Treatment

1- Symptoms may improve by **low-fat diet** supplement with medium-chain triglycerides & vitamins A,D,E & K.

Food allergy

Definition

1- **Immune-mediated disorders**, commonly due to IgE antibodies & type I hypersensitivity reaction caused by ingestion of certain foods
2- **The most common culprits** are peanuts, milk, eggs, soya & shellfish

Clinical features: varies from trivial to life-threatening manifestations

1- Nausea, vomiting, diarrhea & abdominal colic.

2- Urticaria & anaphylaxis
3- The common oral allergy syndrome results from contact with benzoic acid in certain fresh fruit juice leading to urticaria, angioedema of lips & oropharynx

Investigations

1- **Skin-prick test** & measurement of **IgE antibodies** in serum have limited predictive value

Treatment

1- Strict elimination diets
2- Antihistaminics or sodium chromoglycate
3- Treatment of anaphylaxis:
  - Airway support
  - Resuscitation by IV fluids & epinephrine

Lactose intolerance

Definition

1- Lactase enzyme deficiency **leading to** drawback following lactose-containing products i.e. intolerance to milk (lactase hydrolyze milk lactose to glucose and galactose)
2- In most population enterocyte lactase activity declines during childhood
3- The enzyme is deficient in up to 90% of adult Africans, Asians & South Americans, but only 5% of northern Europeans

Pathophysiology

1- In primary lactase deficiency "genetically-determined": jejunal morphology is normal
2- In secondary lactase deficiency: due to celiac disease or viral gastroenteritis there may be villous atrophy
3- Unhydrolysed lactose (osmotic cathartic) passes to the colon, gets fermented by bacteria into lactic acid, volatile short-chain fatty acids, hydrogen & CO_2.

Clinical features

1- Asymptomatic

2- Abdominal colicky pain, distension, increased flatus, borborygmi & watery diarrhea within minutes after ingestion of milk or milk products

Investigations

1- Lactose hydrogen breath test is useful non-invasive confirmatory investigation

Treatment → lactose-free diet or lactose free milk

Dermatitis herpetiform

Characters

1- Crops of intensely **itching blisters** on elbow, knee, back & buttocks
2- Almost all patients have **partial villous atrophy**, even though they usually have no GIT symptoms
3- About 10% of patients with celiac disease have evidence of dermatitis herpetiformis
4- The rash usually **responds to gluten-free diet**, only some patients may requires additional treatment with dapsone (100-150 mg/day).

Zollinger-Ellison syndrome (Gastrinoma)

Definition

1- It's a rare condition characterized by **a triad** of severe peptic ulceration, acid hypersecretion & tumor of non-beta cells of pancreas (gastrinoma)
2- It probably accounts for **0.1%** of all duodenal ulcers

Pathophysiology

1- The tumor secretes large amounts of gastrin, leading to:
  - Increased acid secretion
  - Increased parietal cell mass 3-6 folds

2- Pancreatic lipase is inactivated and bile acids are precipitated → diarrhea & steatorrhea

3- **About 90%** of the tumor occurs in pancreatic head (G cells) or proximal duodenal wall
4- **About 1/2 – 2/3** of the tumors are malignant but are often slow-growing
5- **Associated** adenoma of parathyroid & pituitary glands are present in 20-60% i.e. (multiple endocrine neoplasia MEN-1).

Clinical features

1- **Peptic ulcers in unusual locations** usually such as post-bulbar duodenum, jejunum or esophagus, with poor response to standard ulcer therapy (the ulcers are large, deep and multiple)
2- **Ulcer complications** are common (e.g. bleeding, perforation)
3- **Diarrhea** can be the presenting feature (low PH in upper intestine)

Investigations

1- **Serum gastrin level:** elevated (10-1000 fold).
2- **Secretin injection test:**
    - Normally → no effect or slight decrease in circulating gastrin
    - In Zollinger-Ellison syndrome → paradoxical dramatic increase of circulating gastrin
3- **Tumor localization by**
    - Esophageal U/S
    - Radio-labeled somatostatin scintigraphy
    - CT
4- **Upper endoscopy and small bowel X-ray series**
    - Peptic ulceration in the stomach, duodenum or proximal small intestine
    - Non specific malabsorption pattern

Treatment

1- **Surgical**
    - Tumor resection
    - Highly selective vagotomy lessens the requirement for H2 antagonists in many patients, but the use of PPIs has decreased the need for this operation
2- **Medical**

- High-dose PPIs or H2 antagonists
    - Omeprazole 60-80mg/day, pantoprazole 80-160 mg/day
    - Ranitidine 1,200 mg/day in divided doses. Some patients may require up to 6 g per day
- Synthetic somatostatin analogue (octereotide) give by subcutaneous injection → reduces gastrin secretion & is sometimes of value.

Prognosis and follow up

1- The tumor is **malignant** and the patient dies from malignancy rather than gastrointestinal problems

2- Overall 5-year survival is 60-75%.

3- All patients should be **monitored** for later developments of other manifestations of MEN-1 (e.g. hyperparathyroidism or pituitary tumor)

LARGE BOWEL DISORDERS

Colonic polyps

Definition

1- Polyp is any visible mass protruding from the wall into the lumen of the gut.

2- However it is customary to use the term polyp for **small protrusions** and the term mass for big protrusions.

Classifications

1- **Benign neoplastic Polyps:**

- Adenomatous polyps and polyposis (neoplastic polyps of epithelial origin):
  - Tubular adenoma.
  - Villous adenoma.
  - Tubulovillous adenoma.
- Neoplastic polyps of non – epithelial origin:
  - Lieomyoma.
  - Lipoma and lipomatosis.
  - Haemangioma (Papillary and Cavernous).

2- **Non- neoplastic polyp**

- Hyperplastic epithelial polyps (metaplastic).
- Hyperplastic lymphoid polyps.
- Inflammatory polyps and polyposis.
- Hamartomatous polyps and polyposis.

√√ *The common polyps in Egypt (about 95% from benign polyps):*

1- Adenomatous polyps.
2- Hyperplastic epithelial polyps.
3- Bilharzial inflammatory polyp.

Types and pathology

1- **Common neoplastic polyps (Adenomas):**

- Malignant transformation:
  - 5% of tubular adenomas
  - Tubulovillous adenomas are intermediate
  - 50% of villous adenoma
- Frequency:
  - Tubular adenomas are much commoner than villous adenomas
  - Tubulovillous adenomas are intermediate in frequency

- Microscopically:
    - Tubular: Abnormal tubular glands embedded in the lamina propia (inward growth). Found in any part of large intestine.
    - Villous: Delicate epithelial villiform protrusions that simulate the villi of small intestine (outward growth). Mostly in the rectum
- Macroscopically:
    - Tubular: Dome-shaped, often pedunculated and covered by intact mucosa of dark and reddish color.
    - Villous:

      © Usually sessile, with a broad progressive base that may involve the whole circumference of the rectum reaching a big size up to 12 cm.

      © It is so soft that a mass in the lower rectum is easily missed by digital exam, and so friable as to be often partly shaved off by the proctoscope.
- Because of these characters they do not cause intestinal obstruction even when they reach a big size.
- Localized firm areas within the tumor ↑ suspicion of malignancy.
- Multiple adenomatous polyps occur in 3 syndromes, *Familial adenomatous polyposis, Gardner's syndrome, Turcot syndrome* in these syndromes, the number of polyps may reach several thousands and they are all liable to malignant change, the polyps may involve the colon wholly or partially.

2- Common non-neoplastic polyps:

- Hyperplastic epithelial polyps:
    - Very common.
    - Hyperplasia indicates predominance of proliferation over degeneration.
    - When hyperplasia occurs only in a single focus it causes elevation of the mucous membrane over that focus and formation of polyp.

    - Hyperplastic polyps do not change into adenoma or adenocarcinoma.
    - Macroscopically: often minute, sessile, well-circumscribed and covered by intact mucosa of pale reddish color. Their color is paler than the surrounding mucosa in contrast to adenoma which is darker.

- Bilharzial inflammatory polyps:
    - Cause: Deposition of bilharzial ova in the submucosa and stimulation of a granulomatous reaction around (the connective tissue is loose and allows intense granuloma formation) forming polyps or sandy patches or both.
    - Less common causes: Ulcerative colitis, crohn's disease, shigellosis.
    - Macroscopically: Polyps vary in size from small pea to a large cauliflower mass simulating carcinoma but they never turn malignant. The overlying mucosa is thickened, elevated, and granular.
    - In multiple schistosomal polyposis colic is reported in approx. 5% of schistosomal cases.

3- Rare neoplastic polyps:

- Leiomyoma:
    - Benign tumor of smooth muscle origin
    - Mostly in the rectum
- Lipoma:
    - Mature adipose tissue supported by fibrous stroma and derived from the submucosa
    - Mostly in cecum and region of the ileocecal valve
- Hemangiomas:
    - May be solitary or part of generalized vascular malformation
    - Papillary type → occur in perianal region

- Cavernous type → composed of large blood spaces lined by endothelium and may reach a large size- it is plum colored or reddish colored and often irregular but well circumscribed
- It is important to suspect their presence because biopsy and polypectomy of these tumors may cause fatal Hge and perforation

4- Rare non-neoplastic polyps

- Hamartomatous polyps
  - Non-neoplastic growth: that contains a haphazard mixture of the tissues of the organ from which it arises (developmental defect mostly in children)
  - Juvenile polyps:

    © Mostly < 10 yr

    © Commonest site is the rectum which frequently prolapses at the anus attracting the attention of the mother

    © Pedanculated, round and cherry red in color
- Hamartomatous polyposis:
  - Occur in familial juvenile polyposis, Peutz-Jeghard's syndrome and Cronkhite-Canada syndrome → in these syndromes the polyps involve other parts of the gut esp. stomach and small intestine
- Lipoid hyperplastic polyps
  - Almost in rectum (rectal tonsil)
  - Usually sessile with smooth surface and whitish color
  - Microscopically: contain lymph follicles with large germinal centers, very rarely they become diffuse and multiple

Clinical presentations [prevalence 50% in people > 50yr]

1- Asymptomatic cases

- Most patients with solitary or few polyps are asymptomatic
- They discovered accidentally during barium enema or colonoscopy
- Persons > 40 yrs: should be periodically screened by proctosigmoioscopy or even barium enema esp. with +ve family history

2- Symptomatic cases

- If larger polyps > 1 cm or if complications occur
- The commonest symptom → rectal bleeding (occult or gross), blood bright red and rarely profuse
- Diarrhea: often occur with large villous adenomas, may be profuse with massive water and electrolyte loss
- Sometimes, abdominal colics and cramps (peristaltic contractions)

Complications

1- **Malignant change:**

- Types: adenoma → adenocarcinoma & leiomyoma → leiomyosarcoma
- Villous adenoma > tubular adenoma
- Fact: most if not all anorectal cancers arise on top of preexisting adenomas
- Early change: focal, mostly on the tip of the adenoma
- Simple biopsy: not sufficient to exclude carcinoma and the whole polyp should be removed by colonoscopic polypectomy whenever available as carcinoma may found in polyps as small as 0.5 – 1 cm

Polyp size	Risk of cancer (%)
< 1 cm	0 – 2
1 – 2 cm	10 – 20
> 2 cm	30 – 50

2- **Intussusception**

- Occasionally with large polyps esp. lipomas and adenomas
- Commoner with tumors of the small intestine than tumors of the colon because the colon is more firmly fixed to the posterior abdominal wall with wider lumen

3- **Rectal prolapse**

- Usually with juvenile polyps which may be complicated by bleeding and auto amputation

4- **Massive bleeding**

- Rare, occasionally due to manipulation of a large cavernous hemangioma

Investigations

1- **Proctosigmoidoscopy:**
   - Detect rectal and lower sigmoid polyps (the lower 22-25 cm) which constitute 50% of all colonic polyps
   - Used as screening test for asymptomatic patients > 40 yrs

2- **Colonoscopy : for all cases**
   - The distribution of polyps as follows:
     - 50% in the rectosigmoid
     - 25% in the descending colon
     - 15% in cecum and ascending colon
     - 10% in the transverse colon
   - If polyps present → endoscopic polypectomy with caution if hemangioma is suspected

3- **Barium enema**
   - The double contrast technique with insufflation should be used so as not to miss small polyps

Treatment

1- **Colonoscopic polypectomy:**
   - The treatment of choice for discrete pedunculated polyps
   - Nearly all polyps can be removed
   - Done by encircling the polyp with a wire snare through which an electrocauterizing current is passed
   - Sessile polyps may be removed in a piecemeal fashion
   - Injection of saline to the base of sessile lesion before snaring may give better visualization and complete removal
   - If the polyp is too large to be removed it should be adequately biopsied

2- **Careful histologic examination of resected polyps**
   - Non adenomatous polyps: have little or no malignant potential , so removal of these polyps is sufficient treatment

- Adenomatous polyps: not only predispose to malignancy but also may contain cancer at the time of removal, so all polyps esp. > 1 cm should be examined carefully for adenocarcinoma

3- **Surgical resection indications**

- Malignancy shown by simple biopsy or polypectomy biopsy
- Suspected hemangioma
- Familial adenomatous polyposis and other syndromes (resection of the whole colon)

4- **Diagnosis and treatment of cancerous adenomatous polyps**

Extent of involvement of polyp by cancer	**Implication**	**Recommendations**
Cancer involves only the mucosa without penetration of muscularis mucosa (carcinoma in situ)	The cancer has been cured by polypectomy	- Surgery not indicated - Repeat colonoscopy in 1 yr
Cancer (moderately or well differentiated) has penetrated the muscularis mucosa but does not involve blood vessels or lymphatic in the stalk	The cancer probably has been cured	- Surgery not indicated because the surgical risk outweights the risk of residual cancer - Repeat colonoscopy in 1 yr
Cancer has penetrated the muscularis mucosa and involves blood vessels or lymphatics **or** the cancer is poorly differentiated, whether or not it involves blood vessels or lymphatics	Residual cancer may be present in the colon	- Segmental colon resection is indicated if the patient fit for operation - If residual cancer found at surgery, repeat colonoscopy in 3-6 mo - If no residual cancer, repeat in 6-12 mo
Cancer involves the resectional margin of the polyp stalk	Cancer remains in the bowel	- Segmental colon resection if fit - Repeat colonoscopy in 3-6 mo

Familial adenomatous polyposis (FAP)

Definition

1- It is **autosomal dominant disease** characterized by adenomas of the colon (neoplastic polyposis)
2- When osteomas of the mandible associated with fibromas, sebaceous cysts and colonic polyps → **Gardner's syndrome**

Pathology

1- There are ≥ 100 adenomas in the colon
2- Usually 1000 and sometimes 500
3- The rectum usually involved
4- The polyps appear at adolescence (1st 3 decades)
5- **Malignant transformation** occur within 15 yr in 100% of patients
6- The patient usually dies before the age of 40 yr
7- Associated with duodenum polyps (3-5%) & pancreatic, thyroid cancer and hepatoblastoma (2%)

Clinical features

1- Usually at the age of **30yr**
2- **Abdominal pain**
3- Diarrhea, blood and mucus in the stool

Investigations

1- **Barium enema:** multiple small filling defects throught the colon
2- **Upper endoscopy:** as gastric, duodenal and periampullary polyps are also common
3- **Yearly colonoscopy:** begin at the age of 10 yr in asymptomatic individuals carrying the gene fore FAP

Treatment

1- **Total proctocolectomy (the better):** with an ileostomy or an anal sphincter saving procedure
2- **Total colectomy + ileorectal anastomosis:** not preferred because it requires long term follow up for rectal polyps
3- **Genetic testing:** for family members

Polyposis syndromes

Syndrome	Histology	Location of polyps	Association	Cancer risk
Familial polyposis	Adenomas	- Colon primarily: - Also, stomach & small bowel	- Osteoma of the mandible	Yes
Gardner's syndrome	Adenomas	- Colon primarily: - Also, stomach & small bowel	- Osteomas of mandible, skull and long bones - SC fibromas, lipomas, epidermoid cysts, exostoses, mesenteric fibromatosis, supernumerary teeth, thyroid and adrenal carcinoma	Yes
Turcot's syndrome	Adenomas	Colon	Brain tumors	Yes
Peutz-jeghers syndrome	Hamartomas	Small bowel primarily: also, stomach and colon	- Pigmented plaques of buccal mucosa, hands, feet and perianal skin - Bladder and nasal polyps	Yes (low risk < 3%)
Juvenile polyposis	Hamartomas Adenomas	- Colon primarily: - Also, stomach & small bowel	------------------------	Rare
Neurofibromatosis (von Reckling hausen's disease)	Neurofibromas	Stomach and small bowel	Neurofibromas of skin	No
CronKhite-canada syndrome	Inflammatory	Small bowel primarily: also, stomach and colon	Alopecia , hyper pigmentation and dystrophic nails	No

Ulcerative colitis

Definition

1- Chronic idiopathic disease of the rectal or the colorectal mucosa

2- Characterized by diffuse friability and ulceration **without skip areas** with tendency to formation of pseudopolyps

3- The histological landmark is the **crypt abscess or crypt distortion**

Etiology [completely idiopathic but theories]

1- **Familial:** the condition is more common among relatives of the patients than in the general population (10 – 15%)

2- **Genetic:** there is HLA-B27 relation in patients with IBS and ankylosing spondylitis

3- **Immunologic mechanism**

4- **Diet:** high sugar intake found in crohn's disease, smoking is protective in UC but worsens crohn's disease

5- **Stress** and emotional upset

6- Infective agent?

Pathology

1- **Site of involvement:**

- It can affect the rectum alone (proctitis) or extends proximally to involve the sigmoid and descending colon
- May involve the whole colon
- Inflammation of the distal terminal ileum may occur (backwash ileitis)

2- **Macroscopic changes**

- Diffuse inflammation limited to the mucosa
- Extensive ulceration with no skip areas
- Adjacent mucosa appearing as inflammatory polyps
- Diffuse hypertrophy of muscularis mucosa and propria leading to loss of colonic haustral contractions and water loss
- The mucosal ulceration
  - First tiny and microscopic, then becomes larger and can bee seen
  - The affected mucosa is firely red, granular, friable and bleeds easily on touch. Blood may also ooze from the inflammed mucosa spontaneously due to ↑ vascularity
  - In chronic cases, the mucosa becomes pale, flat and atrophic

3- **Microscopic changes**

- Acute phase:
  - Surface ulceration
  - PMN infiltration of the lamina propria
  - Goblet cell depletion
  - Crypt abscesses
- Chronic phase:
  - Surface regeneration
  - Polypoid formation
  - Mononuclear infiltration of lamina propria
  - Mucosal atrophy and gross distortion of the crypts

Clinical features

1- **Age:** any age (but most common between 20 – 40 yr)

2- **Sex:** females > males

3- **Chronic dysentery:**

- Bloody diarrhea + excessive mucus + tenesmus
- Frequent urge and sense of incomplete evacuation
- The diarrhea characteristically contains little fecal material and varies from 4 – 6 motion/day
- In limited ulcerative proctitis → no diarrhea & constipation predominates
- Abdominal exam. → slight abdominal distension or tenderness
- PR examination is painful and reveals blood (perianal lesions are rare in contrast to crohn's disease)
- Types of dysentery:
  - Chronic continuous type → > 6 months
  - Chronic recurrent type → episodes of 4-12 weeks with symptom free periods in between
- A common misdiagnosis: is to attribute the dysentery of UC or even of cancer colon to amebiasis simply because the stool analysis may contain E.histolytica cysts. E.histolytica is endemic in Egypt and most patients

are simple carriers or cyst passers. So, proctosigmoidoscopy and biopsy should be done esp. if no response to antiamebic therapy

4- Bleeding per rectum

- Minor bleeding: very common early and may mistaken for piles
- Massive bleeding (bleeding which requires > 4 u blood transfusion): uncommon (5%)
- Should be differentiated from diverticulosis coli and angiomatous malformation

5- Chronic secretory diarrhea

- Chronic non bloody diarrhea: may be the presenting symptom
- Continuous or intermittent
- No dysentery or minimal
- ± abdominal colic relieved by defecation
- Examination of the abdomen may show palpable rigid left colon
- Cause: defective water absorption in the colon due to loss of haustral contractions (usually long segment involvement)
- DD: irritable bowel syndrome when bleeding occur

6- Toxic megacolon and perforation

- Incidence: < 5% of cases as late complication or initial presentation
- Risk factors:
    - Prolonged use of anticholinergic or tricyclic antidepressant drugs → megacolon
    - Preparations for barium enema or colonoscopy in megacolon → perforation
- Pathology: all layers of the colon with desquamation of large areas of the mucosa
- Clinical picture:
    - Massive bleeding per rectum
    - Toxic look, dehydration ± shock ± mental confusion
    - Abdominal distension and generalized tenderness
    - If peritonitis → rigidity or rebound tenderness

    - History of diarrhea for a short time before the attack and diarrhea disappears with megacolon. Recurrence of diarrhea is a sign of improvement
- Investigations:
    - Plain X-ray → generalized distension and loss of haustrations
    - Air under the diaphragm → perforation
    - Hypokalemia and hypoalbuminemia → ptn losing enteropathy
- DD:
    - Crohn's disease / acute amebiasis
    - Ischemic colitis / salmonellosis

7- **Extraintestinal manifestations of IBD [10-15%]**

- Joints
    - Peripheral arthritis
    - Sacroiliitis
    - Ankylosing spondylitis
- Skin
    - Erythema nodosum
    - Pyoderma gangrenosum
- Eye
    - Conjunctivitis
    - Iritis
    - Episcleritis
- Liver
    - Fatty infiltration
    - Chronic active hepatitis and cirrhosis
    - Pericholangitis
    - Sclerosing cholangitis
    - Bile duct carcinoma
- Kidneys
    - Pyelonephritis
    - Renal stones

- General
    - Clubbing of the fingers
    - Amyloidosis
    - Anemia
    - Hypercoagulable state
- Conditions related to crohn's disease only
    - Gall stones
    - Renal oxylat stones
    - Obstructive hydronephrosis
    - Vitamin B12 ↓
    - Malabsorption

> **Peripheral arthritis (colitic arthritis)** → characteristically flares with the activity of the disease and subsides with remissions. Have sudden onset with predilection for large joints, migratory course and complete recovery

Complications

1- **Massive bleeding:** delayed complication or early presentation → anemia

2- **Toxic megacolon:** more common in UC

3- **Perforation** → abscess and peritonitis

4- **Benign strictures**

- Less common than in crohn's disease (in crohn's: stricture of small intestine and short gut syndrome)
- Occur with extensive and long standing disease > the acute or limited disease
- Due to muscle abnormality rather than due to fibrosis unlike crohn's disease

5- **Colonic carcinoma**

- More common than in crohn's disease
- Mostly with pancolitis > 7 yrs duration
- Pseudopolyps → not precancerous
- Epithelial dysplasia may be found early in colonoscopic biopsies

- Some consider total colectomy for a high degree dysplasia before cancer development

Investigations

1- **Stool examination and culture**

- To exclude other causes of diarrhea

2- **Blood examinations**

- Anemia of chronic disease (normocytic normochromic)
- ↑ ESR,CRP and TLC → during exacerbation

3- **Barium enema**

- Value:
  - Assess the extent of the disease
  - Visualize local complications as stenosis or cancer
- Contraindications:
  - Severely ill patients
  - Severe bloody diarrhea
  - If toxic megacolon cannot be excluded (done by normal saline)
  - 5 days after proctosigmoidoscopic biopsy
- Characteristics: [usually in rectosigmoid]
  - Mucosal ulcerations, granularity, pseudopolyps, loss of haustration
  - In chronic cases → lead pipe appearance (the colon is narrowed, shortened and uncoiled)
  - Diffuse continuous lesions without skip areas
  - Backwash ileitis (in 10% of cases) → ileocecal valve gaping & the terminal ileum is dilated, stiff and immotile

4- **Proctosigmoidoscopy**

- No prior preparation: as laxatives and enemas → increase inflammation and may lead to perforation
- Value: diagnostic in 100% of cases as rectum is involved in all cases of UC
- The endoscopic appearance of UC:

- The mucosa is edematous & show diffuse granularity, friability and bleeds with exudates
- Ulcers and pseudopolyps esp. in the region of valves of Housten

- Biopsy:
  - Surface ulcerations
  - Infiltration of lamina propria by inflammatory cells
  - Crypt abscesses
- Repeat endoscopy → to assess the course and response to treatment
- DD:
  - Combined granularity and friability

    © Bilharzial colitis

    © Acute bacillary dysentery

    © Campylobacter enterocolitis

    © Radiation proctitis

    → history + self limited condition differentiate
  - Acute amebic dysentery → punched-out ulcers with normal mucosa in between

Stage	Surface	Friability	Exudate
1	Ground glass	Erythematous pin-point spots	Nil
2	Fine granularity	Bleeding pin-point spots	Mucoid
3	Coarse granularity	Diffuse oozing	Mucopurulent
4	Denuded with hyperplastic islands	Diffuse bleeding	Sanguinopurulent

5- Colonoscopy

- Useful in follow up than in initial diagnosis esp. in cancer surveillance
- Sometimes important to exclude crohn's disease

6- Plain X-ray of the abdomen

- Indicated in → acute fulminant colitis or toxic megacolon
- UC → the mucosal edge is seen fuzzy and granular with loss of haustrations

- Toxic megacolon → best seen in transverse colon which is > 5.5 cm width (continuous column of air throughout the entire colon)
- Perforation → free air within the peritoneum
- Impending perforation → air within the wall of the colon itself

Differential diagnosis of IBD

1- **Bacterial colitis**
    - Campylobacter
    - Shigella
    - Salmonella
    - E.coli (invasive)

2- **C.difficile associated colitis**

3- **Parasitic colitis**
    - Amebiasis
    - Schistosomiasis

4- Ischemic colitis

5- Radiation colitis

6- Behcet's colitis

7- **Sexually transmitted colitis**
    - Gonococcus
    - Chlamydia
    - Herpes
    - Trauma

8- **Crohn's disease look- alike**
    - Lymphoma
    - Yersinia
    - T.B

Treatment

General measures

1- Diet: low residue diet & restrict fibers during activity

2- Iron supplement: for anemia

3- Blood transfusion: in severe bleeding

4- Fluid therapy: for dehydration and electrolyte disturbances

Medical treatment [↓↓ inflammation and may cause remission in mild cases]

1- [5 – Aminosalicylic acid]:

- Forms:
    - Available either in a pure form (mesalazine) or in conjugation with sulfapyridine - carrier- (sulfasalazine or salazopyrine)
    - This combination is broken down in the colon by bacteria to release the active agent 5-ASA which acts locally
    - Oral 5-ASA (pure) only not effective because it is absorbed from the small intestine and not reach the colon
- Mechanism: ↓ local PGs synthesis
- Side effects:
    - Abdominal discomfort, so given after eating
    - Folate ↓ (competition between folate and sulfasalazine for absorption)
    - Skin eruption and bone marrow depression
- Initial treatment:
    - 1 g → to minimize gastrointestinal side effects
    - 3 – 4 gm/day → for 2 -3 months or until symptoms controlled
    - CBC and liver enzymes → before therapy and every 1-3 mo initially the every 6-12 mo during long term treatment
- Maintenance treatment:
    - 2 gm/day for 2 years or indefinitely
    - Some may benefit from 1 gm/day
    - ↓ frequency of exacerbations of UC and in mild cases may induce remission
- Preparations and dosage:
    - Sulfasalazine tab. 500 mg [3-4gm/day then 2gm/day]
    - Mesalazine tab. 500mg [1.5gm/day divided in 3 doses – no role]

    - Mesalazine enema 4 gm [once daily at bed time – can reach up to splenic flexure-]
    - Mesalazine supp. 250&500 mg → for ulcerative proctitis [500mg 3 times daily for acute attacks & 250mg 3 times daily for maintenance]

2- **Corticosteroids** [during acute attacks only ± 5ASA]

- Mild attacks and proctitis → local rectal steroids as retention enemas (budesonide enema)
- Moderate attacks → oral prednisone in a dose of 30-40 mg/day with gradual tapering over several weeks to 20 mg/day or less
- Severe attacks and fulminant cases ± toxic megacolon:
    - Hydrocortisone I.V. in a dose of 100-400 mg/day for 48-72 hrs
    - Methylprednisolone I.V. in a dose of 10-30 mg / 6-8 hr
    - Then shift to oral prednisone (60 mg/day)

3- **Immunosuppressive drugs**

- Azathioprine (Imuran) → in cases not responding to steroids (frequent relapse)
- Cyclosporines → should be tried before advocating colectomy

4- **Antidiarrheal agents**

- Diphenoxylate and loperamide → used as adjunctive drugs to control diarrhea
- Habit forming, so long term use is avoided

5- **Antibiotics**

- Metronidazole + ciprofloxacin → for 2ry bacterial infection and septicemia with gram –ve bacteria

Surgical treatment

1- **Indications**

- Acute fulminant attack not responsive to treatment within 2-4 days
- Toxic megacolon or perforation
- Massive bleeding
- Chronicity with poor response to treatment (commonest indication)

2- **Precautions**

- Hyperalimenation or TPN for several days before and after surgery

3- **Operation of choice**

- Total colectomy (proctocolectomy) with permanent terminal ileostomy
- Or subtotal colectomy with ileorectal anastomosis

Medical treatment of fulminant UC

1- I.V. fluids
2- Blood transfusion
3- Antibiotics
4- Nutritional support
5- I.V. cyclosporine or infliximab
6- I.V. methylprednisolone 60 mg/day
7- Heparin → for prophylaxis of venous thrombosis

Crohn's disease

Definition

1- Idiopathic inflammatory bowel disease that **starts in the submucosa** and affects any part of the gut from the mouth to the anal canal

2- It is characterized by **skip areas** in between the affected segments and tendency for invasion of extraintestinal sites as the skin, joints, liver, eyes…

3- **No cure** is available and post surgical recurrence is the rule

Etiology [as before + more in smokers + usually young adults]

Pathology

1- **Site of involvement:**

- Any part of Git from the mouse to the anus
- More common in terminal ileum and ascending colon
- Skip lesions: affection of multiple areas with relatively normal bowel in between
- May involve the whole colon

- Crohn's disease extends from the right colon distally (aborally) while UC extends from the rectum proximally (orally) – sparing of rectum in 50% of cases in crohn's disease-
- Lesions started in the submucous layer and extends both internally to mucosa, externally to serosa and adjacent organs

2- **Macroscopic**

- The involved small bowel usually thickened and narrowed
- Superficial or deep ulcers & fissures in the mucosa → giving a cobblestone appearance
- Fistulas and abscesses may occur → perineal, enterovesical, enterovaginal, enteroenteric and enterocolic fistulas
- Strictures due to fibrosis
- Palpable mass (massive fibrosis → matt several segments of bowel together with the mesentery)

3- **Microscopic** [Transmural affection = all layers]

- Sarcoid- like granulomas
  - Only in 60% of patients, may occur in other diseases
  - Granuloma composed of: collection of epithelioid cells ± giant cells of langhan's type, central caseation does not occur, the granuloma surrounded by a thin ring of lymphocytes
- Lymphocytic hyperplasia (lymphoid follicles)
  - Present in 100% of cases
  - Collections of lymphocytes, sometimes with germinal centers scattered throughout the bowel wall in a transmural distribution

Clinical types

Clinical manifestations depends upon the location and the extent of the disease which vary from one patient to another

1- **Ileo colonic disease:**

- Site and %: ileum alone, colon alone or both. (100% of cases)
- Symptoms:

  - Characteristic triad of (chronic diarrhea + abdominal pain + weight loss) in addition to constitutional symptoms (low grade fever, malaise, nausea and vomiting)
  - Bleeding per rectum → if colonic predominant
  - Perianal lesions are frequent
- Abd. Exam. → often normal or tenderness and right iliac fossa mass may be present
- Complications: intestinal obstruction, toxic megacolon and extraintestinal involvement

2- **Rectal disease**

- Site and %: rectum in 50% of cases (the only site in almost 10%)
- Symptoms → dysentery like symptoms as UC but perianal lesions present in > 50% of cases suggest the diagnosis of crohn's disease

3- **Appendicular disease**

- Site and %: appendex+ adjacent ileum in 50% of cases (but may occur as an isolated lesion)
- Symptoms
  - Acute right iliac fossa pain (as acute appendicitis) ± abscess or cecal mass
  - Usually diagnosed at surgery
  - The condition is also similar to terminal ileitis caused by yersinia

4- **Diffuse small bowel disease**

- Fistulas and obstruction
- Malabsorption and steatorrhea
- Hypoalbuminemia and protein losing enteropathy
- Gall stones and renal stones

5- **Gastroduodenal disease**

- Site and %: uncommon < 4%
- Symptoms → ulcer dyspepsia or gastric outlet obstruction
- Barium meal → tubular narrowing of the antrum with deformity
- Upper endoscopy → cobble stone appearance and duodenal ulcers

6- **Oro-dental type**

  - Site and %: 5 – 20%
  - Presentation → aphthous ulcers of the mouth, diffuse swelling of lips and gums, cobble stone fissuring of the tongue, periodontal abscess, gingival bleeding and teeth mobility

7- **Extraintestinal manifestations** → as before

Investigations

1- **Barium follow-through** [to visualize from E to IC valve]

  - Stricture of the esophagus
  - Conical contraction of the gastric antrum with rigidity and loss of peristalsis
  - Gastric outlet obstruction
  - Cobble stone appearance of intestinal segment and deep ulceration with skip areas
  - Thickening of the intestinal wall with wide separation of the adjacent loops
  - String sign → excessive narrowing of the terminal ileum

2- **Barium enema** [visualize rectum and colon]

  - Early mucosal lesions → patchy ulcerations and fissures
  - Advanced lesions → strictures and fistulas

3- **Proctosigmoidoscopy** [visualize rectum and distal sigmoid]

  - Sufficient as most cases don't need complete colonoscopy
  - Free rectum + affected sigmoid colon → very suggestive of crohn's but occur in 50% of cases
  - Biopsy → aphthous ulcerations, cobble stone appearance, strictures, on background of normal mucosa
  - In chronic cases → pseudopolups and cancer but less common than UC

4- **Complete colonoscopy** [Not routine, indicated in]

  - Inability to reach diagnosis after barium or proctosigmoidoscopy
  - Radiological demonstration of colonic lesions above the reach of sigmoidoscope esp. filling defects and strictures (to exclude malignancy)

- Localization of bleeding source above the reach of sigmoidoscope
- Preoperative and postoperative evaluation of the whole colon
    - Biopsy should taken from different sites
    - If multiple polyps, biopsy taken from polyps that are big, bleeding, ulcerated or have a different color

Complications

1- **Post surgical recurrence:**
  - More when the ileum is involved than in purely colonic cases
  - May occur in the suture line itself or away from it
  - Latent periods of few years usually exists

2- **Malnutrition**
  - Common complication in chronic cases due to obstruction, fistulas, bacterial overgrowth, malabsorption and protein losing enteropathy

3- **Growth retardation in children**

4- **Benign strictures:** of small intestine and short gut syndrome due to fibrosis

5- Massive bleeding: when a fissuring deep ulcer involves a blood vessel

6- Carcinoma: less frequent than UC, and occur in small or large intestine

7- Toxic megacolon and perforation: less frequent than UC, and when perforation occur leads to abscess formation > free peritonitis

Treatment [incurable – comfort and prolongs life]

1- **General measures** [as before +]
  - Fat soluble vitamins
  - Medium chain triglycerides | terminal ileal involvement and steatorrhea
  - Parenteral vitamin B12
  - Antispasmodic and analgesics → for abdominal pain

2- **Medical treatment [as before]**
  - Sulphasalazine → for colonic involvement (1 gm/8hr)
  - Corticosteroids → for moderate to severe attacks (30-60mg/day-prednisone]
  - Immunosuppressive agents:
    - Helpful to maintain the steroid induced remission

    - Azathioprine and 6-mercaptopurine (more effective than in UC)
    - Azathioprine: 2 – 2.5 mg/kg/day
    - Methotrexate: only in crohn's (25 mg/week I.M.)
- Monoclonal antibodies against TNF (infliximab): i.e. biological therapy5 mg/kg I.V. over 2 hrs at 0,2,6 weeks then maintenance at 8 week
- Antibiotics: have greater role than in UC due to common complications of strictures and fistulas with bacterial overgrowth → can cause healing but recurrence occur after discontinuation
    - Metronidazole (800mg/8hr) + co-trimoxazole (2 tab/12hr) useful in severe perianal disease
    - Metronidazole + ciprofloxacin (500mg/12hr)
- Maintenance of remission:
    - Some patients can come off all therapy??
    - Other require a small dose of steroids and/or long term azathioprine therapy

3- Surgical treatment [In most patients]

- Indications:
    - Failure of medical treatment
    - Treatment of complications as bleeding, obstruction, perforation, fistulas, strictures or abscesses
- Operation
    - Resection and end-to-end anastomosis
    - Stricturoplasty
    - Ileostomy → for ill patients with severe fulminating disease followed by resection within 3 mo to 3 years
- Recurrence → is the rule, within 5 – 6 years

Colorectal cancer

Pathogenesis

1- Incidence :

- CRC is the 2nd and 3rd most prevalent cancer in men and women, respectively, in the United States
- In Egypt, it represents 2 – 6 % of total cancer incidence with male to female ratio of 3: 1 with about 30% diagnosed < 45 yr

2- Predisposing factors

- Advancing age (incidence ↑ > 40yr and doubling every decade)
- Family history of colorectal cancer or polyps
  - > 15% in 1st degree relatives compared to 6% of general population
- High-fat, low-fiber diet
- Bowel disorders
  - Inflammatory bowel disease (ulcerative colitis, Crohn's disease)
  - Adenomatous polyps
  - Some polyposis syndromes

    © Familial polyposis syndrome (100%)

    © Gardener's syndrome

    © Turcot's syndrome

    © Peutz-Jeghers syndrome (< 3%)

    © Juvenile polyposis (rarely)
  - Familial colon cancer syndrome (®)
- Associated genital tract cancer in women (ovaries and uterus) or melanoma
- Associated breast cancer

3- Site

- Any part of the colon
- Rectosigmoid in 45%
- The ascending colon and cecum in 25%

4- Pathology

- Microscopic → adenocarcinoma
- Gross → cauliflower mass, malignant ulcer or infiltrating mass

Clinical presentation

1- lower GI bleeding :

- The most common presenting sign (esp. with recto-sigmoid lesions)
- Bleeding may be gross or occult
- Occult bleeding typically is detected on routine rectal examination or stool screening tests

2- **Change in bowel habit ± abdominal pain:**

- The most common symptom (esp. with left sided colonic lesions)
- May be manifested as a decrease in the caliber of the stool if the lesion is distal and constricts the bowel lumen.
- Patients may complain of constipation.
- Sometimes diarrhea develops around a partially obstructing lesion.

[Unfortunately, these are both late manifestations of the disease i.e. the majority are asymptomatic until advanced stage]

3- **Mass lesions of the ascending colon**

- Because of the larger diameter of the ascending colon and caecum, may grow to a considerable size before symptoms develop.

4- **Other possible consequences include**

- Anorexia, malaise
- Intestinal obstruction
- Enterovesical or enterocutaneous fistula

5- Rarely, the patient may seek treatment initially for **symptoms of metastatic** disease, such as jaundice or bone pain.

6- **Physical examination**

- Weight loss, muscle wasting
- Anemia.
- A mass may be evident in the abdomen or by rectal examination.
- Hepatomegally in liver metastases
- Stool may be positive for gross or occult blood.

Investigations

1- **Laboratory studies**

- CBC → anemia
- Serum iron studies → confirm iron deficiency

- ↑ serum alkaline phosphatase level, if confirmed to originate in the liver either by fractionation or by the finding of an ↑ 5′-nucleotidase → suggests liver metastases
- Sometimes an isolated ↑ of serum LDH or GGT is the only indicator of liver involvement
- ↑serum bilirubin + ↑alkaline phosphatase level → suggests either extensive liver metastases or obstruction of the external bile ducts by metastatic lymph nodes.
- Carcinoembryonic antigen (CEA) :
    - May be ↑ but is not helpful in making a diagnosis
    - Its role is largely confined to the follow-up period after primary treatment of the cancer to monitor for recurrence or metastatic spread.

2- Imaging studies

- Colonoscopy and biopsy:
    - The gold standard for diagnosis of colon polyps or cancer.
    - Polyps amenable for colonoscopic polypectomy are removed
    - Polyps that are too large or too sessile to remove are biopsied for histopathologic evaluation.
- Barium enema, preceded by flexible sigmoidoscopy
    - Historically has been used as the first specific diagnostic study
    - An irregular filling defect or an encircling “apple core” lesion on the barium enema is highly suggestive of adenocarcinoma
- Virtual colonoscopy or CT colography of the colon
    - May be used for screening of the colon for the presence of polyps and cancer; however, it is not yet widely available.
    - If a polyp is seen or suspected, a colonoscopy needs to be performed to confirm its presence and for its removal.

3- Work up for metastatic disease

- CT scan of the chest, abdomen, and pelvis with intravenous contrast

- MRI of the liver may be obtained to assess the number and size of the liver metastases.

Differential diagnosis

[Weight loss, blood in the stool, and a mass in the colon]

1- Adenocarcinoma of the colon.
2- Leiomyosarcoma
3- Lymphoma.
4- Inflammatory mass caused by diverticulitis or amebiasis mimics colon cancer

Histopathologicall differentiation is not difficult

Modified Duke's classification

Dukes' category	Definition	Five-year survival (%) after treatment
A	Cancer limited to mucosa or submucosa	90
B1	Cancer penetrates into but not through the muscularis propria	80
B2	Cancer penetrates through the muscularis propria or the serosa	70
C1	Same as B1 plus lymph node metastases	50
C2	Same as B2 plus lymph node metastases	50
D	Distant metastases	<30

Treatment

1- **Dukes' A, B, and C lesions:** is surgical unless operative risk is prohibitive.
   - **Rectal cancers** usually require an abdominoperineal resection
   - Preoperative chemo radiation therapy of rectal cancers seems to improve surgical and overall outcome.
   - More proximal colon cancers **(left side)** are treated by wide resection of the involved segment with end to end anastomosis
   - **Right sided tumors** are removed by right hemicolectomy
   - Regional lymph nodes also are removed.

2- **Patients with stage D cancers**
   - May require **palliative resection** to control bleeding or to treat or prevent obstruction.

- Preoperative **irradiation**, sometimes in conjunction with **chemotherapy**, has been reported to shift the Dukes' staging to less extensive disease and improve surgical results.
- Radiotherapy of bony metastases may relieve bone pain.
- **Adjuvant chemotherapy** of metastatic colon cancer include :
  - 5-fluorouracil, leucovorin, and irinotecan or
  - A combination of oxiplatin and raltitrexed, Avastin and bevacizumab
- **Liver metastases** may be resected to increase survival

Prognosis

1- The 5-year survival rate is directly related to the extent of tissue invasion, as indicated by the Dukes' classification

2- In addition, prognosis and recurrence are adversely affected when tumors are poorly differentiated.

Recommendations for cancer surveillance and follow up of polyps and cancer

1- Rationale for CRC screening

- Early detection of CRC can improve outcome significantly.
- The 5-year survival rate for patients with stage I to II disease is 80% - 90%, whereas it is 60% for those with stage III disease and < 10% for stage IV disease.
- Most sporadic CRCs arise from adenomatous polyps and the progression from normal mucosa through polyp formation and subsequent development of cancer is a process that occurs over a 5- to 15-year period. Consideration of this time frame is important when deciding what intervals are optimal for repeated screening.

2- Tests available for cancer screening

- Digital rectal examination
  - Most physicians are able to examine the rectum digitally to a depth of 7 - 9 cm.
  - Detect about 5% - 10% of polyps.

    - An infiltrating cancer feels hard and irregular, whereas a benign polyp is more likely to be soft and pliable.

- Test for occult blood in the stool
    - Because bleeding is the most common sign of CRC, testing for occult blood in the stool is valuable in cancer surveillance.
    - Guaiac-impregnated cards have low false-negative and false-positive rates when used properly.
    - Patients should adhere to a special diet for 48 hours before the stool is tested for occult blood. The diet eliminates foods and agents that are likely to give a false-negative or false-positive result but includes "roughage," which is believed to stimulate bleeding from existing bowel lesions.
    - The most reliable method of testing for occult blood is to obtain two smears per day from different parts of the stool for 3 days.
    - Annual fecal occult blood testing reported to decreases the 13-year cumulative mortality from CRC by 33%.
    - Diet for fecal occult blood testing

Avoid	**Include in diet**
Red meat	Chicken
Aspirin and nonsteroidal drugs	Tuna fish
Peroxidase-containing foods (e.g., turnips, horseradish)	Raw or cooked vegetables Fruit
Vitamin C, citrus juices (false-positive)	Bran cereal
Iron-containing drugs (false-positive)	Peanuts
	Popcorn

- Colonoscopy, sigmoidoscopy, barium enema x-ray, CT colographic examination.

3- In general population (algorithm)

4- In patients with colonic polyps (algorithm)

5- For people with a family history of CRC

- People who have a parent, a sibling, or a second-degree relative with colorectal carcinoma are at higher risk of development of CRC, albeit much less than those who have familial colon cancer syndrome.
- People who have one first-degree relative with CRC should undergo colonoscopy starting at age 40, or 10 years before the age of the onset in the affected relative.
- For people with two affected first-degree relatives, or one first-degree relative and one or more second-degree relatives, initial colonoscopy at age 40 may be justified, followed by routine yearly stool occult blood testing and periodic colonoscopy every 3 - 5 years.

6- For postoperative colonoscopic follow-up of patients with resected CRC

- Patients are at greater risk of the development of another colorectal carcinoma.
- Colonoscopy 12 months after surgery to look for recurrence at the anastomosis and elsewhere in the colon.
- Subsequent colonoscopic examinations should be every 2 - 3 years.

7- Chemoprevention of prevention of CRC

- Long-term use of oral agents to prevent the development of adenomatous polyps and their subsequent progression to CRC.
- Recent observations suggest that patients taking inhibitors such as celecoxib, aspirin, NSAIDs, cyclooxygenerase-2 (COX-2), supplemental folate, calcium, and estrogen, as seen in postmenopausal women taking hormone replacement therapy, experience a chemopreventive benefit.
- Other potential chemopreventive agents as ursodiol, eflornithine, and oltipraz are undergoing evaluation in clinical studies.
- Chemoprevention should not replace periodic fecal occult blood tests and endoscopic screening as well as modification in known risk factors of CRC such as reduction in the intake of red meat, appropriate exercise, smoking and alcohol cessation, and weight control.

Familial colon cancer syndrome

1- **Definition**: Hereditary nonpolyposis colorectal cancer (HNPCC) syndrome is a condition that is transmitted in an autosomal dominant fashion with a high degree of penetrance for the development of colorectal carcinoma.

2- Types :

- In type 1, cancers are confined predominantly to the colon.
- In type 2, cancers occur not only in the colon but also in the female genital tract, breast, brain, small bowel, pancreas, lymph system, and bone marrow.

3- **Diagnosis:** is suspected when CRC occurs in a young person with a family history of CRC

4- **Criteria for diagnosis** (modified Amsterdam criteria):

- Three or more relatives with colon cancer (at least one first-degree).
- Colorectal cancer in two or more generations.
- At least one member affected < 50 years of age.
- FAP excluded.

5- Surveillance

- Should begin when family members are age 10 with genetic testing.
- Fecal occult blood should be tested yearly.
- Total colonoscopy should be performed every 3 years beginning at age 20.
- Because of the high prevalence of cancers in the proximal colon, flexible sigmoidoscopy is not sufficient.
- Women with type 2 HNPCC syndrome should undergo yearly pelvic examinations.

6- **Treatment**: if colon cancer is detected, total or subtotal colectomy is indicated

Irritable bowel syndrome

Defintion

1- It is a **functional** bowel disorder in absence of structural pathology
2- It usually an **exaggeration** of normal physiologic responses and possibly heightened perception of pain
3- **Terms** that include the words colon or colitis are inaccurate because the condition is not limited to the colon, and inflammation is not a feature

Incidence → The most common of all digestive disorders (50%)

Pathogenesis (uncertain)

1- **Etiology**
    - Altered bowel motility
    - Increased sensory perception of pain
    - Psychological disturbances
    - Visceral hypersensitivity
    - Abnormality in gut flora
2- **Triggering factors (may)**
    - GI infection
    - Psychological stress
    - Eating disorders
    - Mood disorders
    - Antibiotic therapy
    - Pelvic surgery
3- In many patients IBS may be characterized as **diarrhea predominant (IBS-D)** → hypomotile bowel, **constipation predominant (IBS-C)** → hypertonic segmental contractions, and for some patients, an alternation of diarrhea with constipation (alternators).

Clinical features

Symptoms

1- **Long history** (months to years) with long symptom free intervals and history of several physicians and gastrointestinal evaluations.
2- **Typical symptoms:**
    - Recurrent crampy abdominal pain (classically in left iliac fossa), often relieved temporarily by defecation or passing flatus.

- Constipation with feeling of incomplete evacuation
- Or diarrhea
- Abdominal distention

3- In some patients

- Chronic constipation is punctuated by brief episodes of diarrhea
- Straining or urgency

4- Timing of symptoms

- Symptoms usually correlated with emotional stress, but often such a relation is not evident or becomes apparent only after careful questioning

5- Bowel movements

- Stools may be clustered in the morning or may occur throughout the day, but rarely is the patient awakened at night.
- Stools may be ribbon like with excessive amount of mucus, but blood is not present unless there is incidental bleeding from hemorrhoids.

6- Belching and symptoms of **gastroesophageal reflux and dyspepsia** are common because IBS may affect the entire digestive tract

7- Rome diagnostic criteria:

- Abdominal discomfort or pain that has 2 of 3 of the following features
  - Relieved with defecation and/or
  - Onset associated with a change in frequency of stool (> 3 /day and < 3 /week)
  - Onset associated with a change in the form or appearance of stool (hard, loose, watery or lumpy)

8- Non GI features

- Dysmenorrhoea and premenstrual tension
- Unpleasant taste and bad breath
- Headache, fatigue and poor sleeping
- Urinary symptoms e.g. frequency, urgency

Signs

1- General condition → weight stable or increasing with appearance of health

2- Features of **tense** or anxious person usually present

3- Voluntary **guarding** if abdominal pain present
4- Sometimes, **tender** firm sigmoid colon is palpable
5- A thorough **physical examination including rectal examination** is important in the evaluation for a non-IBS disorder

Differential diagnosis

1- Including most disorders that cause **diarrhea and constipation**
2- **Features againest the diagnosis of IBS:**
    - Anorexia
    - Weight loss
    - Rectal bleeding
    - Fever
    - Nocturnal diarrhea
    - Recent onset of symptoms
3- **In lactose intolerance**
    - Postprandial diarrhea associated with crampy pain
    - Trial of a lactose-free diet usually are sufficient to make diagnosis
4- Celiac sprue, Crohn's disease, and endometriosis also can masquerade as IBS because of the vagueness of the symptoms in many patients.
5- A clinical history of postprandial abdominal pain suggests the possibility of gallbladder, pancreatic, or peptic disease.
6- The physician should remember, however, that other gastrointestinal disorders can develop in patients with IBS, thus one should be alert to a change in the patient's complaints.

Laboratory evaluation of suspected cases

[IBS diagnosed by exclusion of other treatable disorders]

All patients	**Selected patients**
1- Stool for occult blood 2- If diarrhea, stool for leukocytes, ova, parasites or bacterial pathogens 3- CBC and ESR	1- U/S for gallbladder 2- Abd.and pelvic CT 3- Serum amylase level 4- Lactose tolerance test 5- If blood in stool → UGI endoscopy and colonoscopy

	6- Colonic mucosal biopsy → lymphocytic and collagenous colitis 7- Small bowel biopsy → celiac, whipple's or crohn's 8- Upper GI series with follow through → crohn's 9- Capsule endoscopy

Treatment

1- **All patients**

- Reassurance and emotional support
- Stress reduction programs
- Judicious use of tricyclic antidepressants and serotonin reuptake inhibitors
    - May be useful in selected patients for the short-term management of situational anxiety and depression
    - Tricyclic antidepressants such as: amitriptyline HCL (10-25mg) or desipramine HCL
    - SSRIs such as: fluoxetine HCL, sertraline HCL, and paroxetine
- The commonsense approach to diet therapy is the most appropriate
    - There is no need for bland or highly restrictive diets
    - Patients should avoid foods that they find cause symptoms.
    - If lactose containing foods produce cramps and diarrhea, these should be eliminated from the diet

2- **Patients with abdominal pain and constipation**

- Increase dietary fiber and bran → relieve symptoms but may result in increase of gas and bloating
- Stool softeners e.g. colace
- Laxatives e.g. lactulose
- Anticholinergics-antispasmodics e.g. dicyclomine HCL 10-20 mg 2-4 times daily (S.E: dry mouth, blurred vision, and urinary retention)
- Lubiprostone (Amitiza):
    - Indicated in treatment of chronic constipation

    - Its mode of action is stimulation of chloride channels of the intestinal mucosal and facilitation of chloride and water secretion into the small-intestinal lumen → increasing the stool fluid content and volume
- Tegaserod (Zelmac) :
    - Serotonin receptor agonist used in IBS-C in female patients up to 65yr (6 mg/12 hr)
    - It facilitates serotonin secretion within GI wall →↑ peristalsis
    - Contraindicated in patients with cardiovascular risk
    - Removed from USA market for further evaluation of its safety in long term use

3- **Patients with diarrhea**

- Increase dietary fiber and bran (may firm watery stools)
- Antidiarrheal agents
    - Diphenoxylate HCL (lomotil), 2.5-5 mg /6hr as needed
    - Loperamide HCL (Imodium), 2mg /6hr as needed → may be preferred for long-term use because of its longer duration of action. Also, it does not cross BBB and thus is less likely to cause addiction
- Low dose tricyclic antidepressants may be helpful
- Anticholinergics-antispasmodics

PANCREATIC DISORDERS

Chronic pancreatitis

Definition

1- Chronic inflammatory disease of the pancreas characterized by progressive **destruction and fibrosis**

2- The exocrine pancreatic tissue and function are lost in the earlier stages followed by loss of endocrine parenchyma and function

Causes and classification

1- Obstructive chronic pancreatitis

- Causes → obstruction of the pancreatic ducts which preceded the onset of pancreatitis
  - Tumor
  - Necrotic pseudocysts
  - Scars of parynchymal inflammation
  - Congenital anomalies as (annular pancreas or pancreas divisum)
  - Hemochromatosis
  - Sjogren's syndrome
- Characters:
  - The ductal epithelium is relatively preserved
  - No intraductal protein plugs or stones

2- Chronic calcifying pancreatitis (CCP)

- Incidence → the most common type (95%)
- Causes:
  - Chronic alcohol consumption (the most important)
  - ↑ by cigarette smoking
  - ↑ by diets high in protein and high or low in fat
  - Hyperparathyroidism and hypercalcemia
  - Some tropical countries → in non alcoholic young adults (12-20yr) living in areas where protein and fat poor diets are consumed [**Tropical pancreatitis**]
  - Hereditary autosomal dominant form of CCP with variable penetrance **[Hereditary pancreatitis]**
- DD → cystic fibrosis
- Pathogenesis:

- Pancreatic lithogenesis involves the precipitation of both a fibrillar protein- a form of pancreatic stone protein psp- and calcium carbonate
- Chronic alcohol → ↑ protein conc. In pancreatic juice and ↓ psp and citrate conc. → ↑ Ca availability & ↑ viscosity of pancreatic juice which leads to formation of protein plugs and calcification

- Morphology:
  - Lobular and patchy distribution of lesions
  - Protein plugs always found in the ductal and acinar lumen
  - Pancreatic calcification (calculi)
  - Atrophy of the epithelium is common
  - Stenosis of the ducts is common
  - Recurrent acute pancreatitis
  - Retention cysts and pseudocysts

Clinical features

1- **Onset** → insidious

2- **Age** → 35 – 50 yr

3- **50%** → present with episodes of acute pancreatitis & 30% → present by only abdominal pain & Others → jaundice, weight loss, DM, upper GI bleeding and malabsorption & 2% → no pain

4- **Abdominal pain:**
- Site: mid epigastrium, may upper abdominal or periumbilical
- Radiation to the back
- Associated with nausea ± vomiting
- ↑ with supine position
- ↓ by sitting up and leaning forward

5- **Marked weight loss:** due to anorexia and malabsorption

6- **Malabsorption:**
- Steatorrhea is often an earlier and more severe problem than azotorrhea because secretion of lipase and colipase decreases earlier than that of the proteolytic enzymes

- Fat and protein
  - Occur when the secretory pancreatic capacity decreased by 90% → steatorrhea
  - ↑ oral intake of protein can compensate the condition without additional abdominal discomfort
  - ↑ oral intake of fat leads to increased diarrhea and abdominal pain
  - Steatorrhea of chronic pancreatitis consists mainly of triglycerides (esterified fats → make the stool volume smaller) in contrast to steatorrhea of sprue which contains FFA
- CHO malabsorption: rare, because loss of 97% of amylase secretion is necessary for maldigestion of starch
- Vitamin B12 malabsorption: may occur in some patients due to ↓ levels of pancratic proteases esp. trypsin, in the duodenal lumen (which separate protein R from vitamin B12). So, the R protein is not cleaved off vitamin B 12 and IF-vitamin B12 complex does not form
- Decreased pancreatic exocrine function does not affect the absorption of bile salts, water or fat soluble vitamins, iron or calcium

7- **Diabetes millitus**

- Incidence : 7%
- Cause : ↓ insulin and glucagon release due to pancreatic calcification
- Hypoglycemia: may develop even with low doses of insulin because of concomitant ↓ glucagon secretion. So, these patients become very sensitive to insulin

8- **Physical examination**

- May be epigastric tenderness
- May be palpable mass if pseudocyst develops
- No signs of fat soluble vitamin deficiency (A,D,E,K)
- Jaundice occur if common bile duct obstruction due to scaring in the pancreatic head (in these patients, it is difficult to differentiate pancreatic cancer from chronic pancreatitis)

Complications

1- **Pancreatic** pseuocyst
2- **Pancreatic** ascites: if communication occur between the pancreatic duct and the peritoneal cavity
3- **Pancreatic** abscess
4- **Obstructive** jaundice
5- Common bile duct **obstruction**
6- Duodenal **obstruction**
7- Portal and splenic vein thrombosis

Investigations

1- **Serum amylase or lipase :** of little value, may not elevated even in acute attacks
2- **Stool fat :**
    - Steatorrhea is best confirmed by 72-hr stool collection for quantitative determination of fat
    - Most patients consuming 100 gm of fat / day excrete > 10 gm of fat /day
    - In advanced pancreatic insufficiency, stool fat may reach 30-40 g/d
3- **Plain X-ray:** show pancreatic calcification in 30% of cases
4- **U/S and CT : show**
    - Abnormalities in pancreatic size
    - Pancreatic calcifications in most cases
    - Pseudocysts, ductal dilatation and tumors
5- **Angiography**
    - If tumor suspected → it shows vascularization
    - If splenic vein thrombosis → it detects the site of occlusion
6- **ERCP**
    - Show dilatation, cystic changes, strictures and calculi
    - Differentiate pancreatic cancer from chronic pancreatitis
        - In cancer, only that part of the duct involved with the tumor is abnormal
        - In pancreatitis, generalized abnormal changes
7- **Estimation of pancreatic exocrine function**
    - Secretin stimulation test

- The lundh test meal
- Bentiromide test

8- **Blood glucose:** if DM is suspected

9- **Cholestatic liver chemistry** : if common bile duct obstruction

Treatment [mainly supportive, directed at the complications]

1- **Management of pain**

- Alcohol and tobacco should be stopped
- Diet : moderate fat and protein and high CHO content
- Small feedings + analgesics may be sufficient
- Narcotics may be required in many patients
- Feed back control : (important esp. in mild to moderate cases), oral treatment with large doses of pancreatic enzymes useful in
  - ↓ abdominal pain by inhibiting the pancreatic exocrine secretion and allowing the pancreas to rest
  - ↓ frequency of acute recurrent pancreatitis
  - Healing of pancreatic fistulas
- Percutaneous injection of alcohol to destroy the celiac plexus → relieve pain in some patients for as long as 6 months
- Surgery : for intractable pain → give short term relieve of pain
  - Drainage : if pancreatic duct dilatation
    © Longitudinal pancreaticojejunostomy (Puestow procedure)
    © Caudal pancreaticojejunostomy (Duval procedure)
    © Sphincteroplasty
  - Partial resection of the gland : if the abnormality is confined to a segment of the pancreas (40-95% of the gland) + no pancreatic duct dilatation

2- **Malabsorption**

- If the steatorrhea > 10 gm of fat / day → pancreatic enzyme supplementation + dietary fat restriction
- If steatorrhea < 10 gm /day → dietary fat restriction only benefit
- Pancreatic enzyme supplements:

- To eliminate malabsorption, the conc. Of enzymes delivered to the duodenum need only to be 5 – 10 % of the conc. That is secreted into the duodenum after maximal stimulation of the pancreas. This means that ≈ 30,000iu of lipase must be present in the duodenum with each meal, most commercial preparations contain only 3,000 – 4,000 u of active lipase per tab.
- Preparations: given before each meal
  √ viokase (8 tab.)   √ cotazym (6 tab)
  √ llozyme (4 cap.)   √ zymase (3 cap.)
- If pancreatic pain present , add one – 2 doses at bedtime
- Side effects of large doses: Nausea, abdominal cramps , perianal excoriation, hyperuricemia and kidney stones esp. in children
- Precaution: pancreatic lipase is irreversibly inactivated by a PH < 4, therefor, it is important to maintain the gastric PH > 4 for at least 1 hr postprandially. So, higher dosages of enzymes or adjuvant acid suppressant therapy or both may be necessary to keep the intragastric PH > 4 to deliver adequate active enzyme conc. To the small bowel

- Adjuvant acid suppressant therapy
  - Sodium bicarbonate and aluminum hydroxide
    © The only antacids effective in ↓ steatorrhea
    © Dose: 16.6 gm/24hr for sodium bicarbonate & 18.4 gm/24hr for aluminum hydroxide
    © Sodium bicarbonate 650 mg before and after meals effective esp. with viokase
  - Other ↑ steatorrhea by precipitating bile salts
  - H2 blockers or PPIs (not given in the same time with enzymes)
  - Enteric PH-coated pancreatic enzyme preparations: as creon are effective if gastric PH remain at 4-5 and the duodenal PH > 6

3- DM: insulin dosage needs to be closely monitored

4- Bacterial overgrowth (in 25%)

  - Tetracycline 500 mg 3-4 times / daily for 7-14 days
  - Metronidazole 250-500 mg 3 times /daily for 7-14 days

5- **Nutritional support**

  - Small frequent meals, high in protein
  - Medium chain triglycerides substituted for long chain triglycerides

Acute pancreatitis

Definition

1- Acute inflammatory process of the pancreas resulting from intrapancreatic activation of digestive enzymes

2- Acute edematous or interstitial pancreatitis

  - Mild and self-limited in most patients.
  - The inflammation results in interstitial edema.
  - The parenchymal damage is minimal, and the organ recovers its function after resolution of the inflammation.

3- Hemorrhagic or necrotizing pancreatitis

  - In some patients, the inflammation may be extensive and progress to coagulation necrosis of the gland and the surrounding tissues, leading to hemorrhagic or necrotizing pancreatitis.
  - The mass of inflamed pancreas containing necrotic tissue is referred to as a phlegmon.

Etiology

1- The 2 most common etiologic factors associated with pancreatitis are **alcoholism** and **biliary tract disease** (gallstones).

2- These two factors account for 75% - 85% of all cases.

1- Alcohol (ethanol, methanol) abuse (acute and chronic alcoholism)
2- Gallstones, biliary sludge (biliary tract disease)
3- Surgery (abdominal, cardiac, cardiopulmonary bypass, thoracic)

4- Trauma (blunt, penetrating)
5- Endoscopic retrograde cholangiopancreatography
6- Infections (viral: mumps, coxsackie, CMV, HSV, HIV; bacterial: Mycoplasma, Legionella, Leptospira; fungal: Aspergillosis; parasitic: Salmonella, Mycobacterium, Toxoplasma, Cryptosporidium)
7- Metabolic disorders (hypertriglyceridemia, pregnancy, hypercalcemia-hyperparathyroidism Vasculitis, ischemia
8- Drugs (see below)
9- Anatomic abnormalities in the area of the ampulla of Vater with possible obstruction (Crohn's disease, duodenal diverticulum, annular pancreas, pancreas divisum, choledochal cyst, sphincter of Oddi dysfunction, ampullary neoplasm, pancreatic neoplasm, ampullary stenosis)
10-Penetrating gastroduodenal ulcer
11-Hereditary autoimmune factors
12-Miscellaneous (scorpion bite, parasites obstructing the pancreatic duct [Ascaris, fluke], severe systemic hypotension, cholesterol embolization, Reye's syndrome, fulminant hepatitis, refeeding in eating disorders)
13-Renal failure
14-Renal transplantation

Drugs definitely associated with Pancreatitis

1- Sulfonamides, sulfasalazine
2- Estrogens (oral contraceptives)
3- Tetracyclines
4- Azathioprine
5- Mercaptopurine
6- Furosemide
7- Thiazides
8- Valproic acid
9- Ethanol
10- Methanol
11- Organophosphate insecticides
12- Pentamidine
13- ACE inhibitors
14- DDI (2,3 dideoxyinosine)

Prognostic factors

1- **In most individuals**, the disease is mild or moderate with full recovery of the patient.
2- However, **in some individuals**, the disease may be fulminant with very high morbidity and mortality.
3- **Mortality** 1% with < 3 Ranson's signs, 10-20% with 3-5 signs and > 50% with > 6 signs
4- Patients at high risk should be treated in an **ICU** and may require **surgical** intervention.

On Admission

Age >55 y
WBC >16,000/µL
Blood glucose >200 mg/dL (no diabetic history)
Serum LDH >350 IU/L (normal up to 225)
SGOT >250 Sigma Frankel units/L (normal up to 40)

Within 48 h

Age >55 y
WBC >15,000/Ml
Blood glucose >180 mg/dL (no diabetic history)
Serum urea >16 mmol/L (no response to IV fluids)
BUN rise >5 mg/dL
PaO_2 <60 mmHg
Serum calcium <8.0 mg/dL
Hematocrit fall >10%
Base deficit >4 mEq/L
Fluid sequestration >6 L
Serum albumin <3.2 gm/dL
Serum LDH >600 units/L (normal up to 255 units/L)
AST or ALT >200 units/L (normal up to 40 units/L)

Clinical Criteria for Severe Pancreatitis

Cardiac	BP <90 mmHg, tachycardia >130, arrhythmia and other ECG changes
Pulmonary	Dyspnea, rales PO_2 <60 mmHg, adult respiratory distress syndrome
Renal	Urine output <50 mL/h, rising BUN and creatinine
Metabolic	Calcium <8 mg/dL, albumin <3.2 g/dL
Hematologic	Falling hematocrit, diffuse intravascular coagulation

Neurologic	Irritability, confusion, CNS localizing signs
Abdominal	Tense distention, fluid wave, ileus

Clinical presentation

Symptoms

1- Abdominal pain:

- The most common complaint
- Site: usually in the epigastrium, left upper quadrant, or periumbilical area
- Radiation: often radiates to the back, chest, flanks, and lower abdomen.
- Character: The pain is steady, dull, and boring
- ↑ When the patient is supine
- ↓ In the sitting position with the trunk flexed forward and the knees drawn up.

2- Nausea, vomiting and abdominal distention secondary to ileus

Physical examination

1- Initially:

- Fever
- Tachycardia
- Hypotension

2- Shock is common in severe instances

3- Jaundice may occur, due to

- Obstructive cholelithiasis
- Or, more commonly, the compression of the intrapancreatic portion of the common bile duct with edema of the head of the pancreas.

4- Abdominal tenderness and rigidity may be present

5- Bowel sounds are diminished or absent.

6- The presence of a bluish discoloration around the umbilicus (**Cullen's sign**) and at the flanks (**Turner's sign**) suggests hemoperitoneum and results from hemorrhagic necrotizing pancreatitis.

7- Other findings may be present such as

- Pleural effusion (especially on the left side)

  - Pneumonitis
  - Other pulmonary findings, such as ARDS, and subcutaneous fat necrosis resembling erythema nodosum may be present.

8- Tetany due to hypocalcemia is a rare finding

Investigations

Laboratory studies

1- Serum amylase

  - ↑ In 75% of the patients
  - ↑ Within the first 24 hours and persists for 3 - 5 days.
  - Amylase levels normalize unless there is:
    - Extensive pancreatic necrosis
    - Pancreatic abscess
    - Ductal obstruction
    - Pseudocyst formation.
  - May be normal in patients with :
    - Hypertriglyceridemia
    - Recurrent alcoholic pancreatitis.

2- Serum lipase

  - ↑ in 70% of patients
  - When both serum amylase and serum lipase are determined, one enzyme is elevated in 80% - 85% of the patients with acute pancreatitis, thus increasing the diagnostic yield.

3- Urine amylase

  - ↑ and may remain elevated for 7 - 10 days after serum levels have returned to normal.

4- Peritoneal aspiration: contains high amylase

5- Leukocytosis (10,000-20, 0000/μL) is frequent.

6- Hematocrit elevation to > 50%

7- Hyperglycemia is not uncommon

8- Hypocalcemia occurs in about 25% of patients.

9- Serum bilirubin, alkaline phosphatase, and ALT, AST levels

- May be transiently ↑
- Return to normal in 4 - 7 days unless there is persistent biliary obstruction from gallstones or other causes.

10- **Arterial hypoxemia** may be present in 25% of patients

Radiologic studies

1- **The plain X- ray films (abdomen, PUT) :**
   - Useful in excluding other diagnoses, such as perforated viscus, mesenteric ischemia, or infarction.
   - May be Pancreatic calcification (acute on top of chronic pancreatitis)
   - Findings suggestive of diffuse or localized ileus and presence of ascites are nonspecific.

2- **US and CT scans**
   - Determines:
     - The size and appearance of the pancreas
     - The peripancreatic spread of the inflammation and phlegmon
     - The condition of the biliary tract
     - Complications such as cholecystitis, choledocholithiasis, tumor, pseudocyst, and ascites.
   - When ileus is present:
     - US waves are scattered by the air in the intestinal lumen, and a clear picture of the pancreas cannot be obtained.
   - However, US is the test of choice for documenting cholelithiasis and biliary ductal dilatation.
   - CT scan of the abdomen:
     - Recommended if severe pancreatitis is suspected (e.g., multiple positive Ranson's signs during the first 48 hours).
     - If the CT scan is normal or shows mild pancreatic edema, the likelihood of a severe complication is remote even if many of Ranson's signs are positive.
   - Findings of necrotizing pancreatitis:
     - Markedly swollen pancreas with or without fluid collections

- The distinction between acute interstitial and necrotizing pancreatitis made by dynamic CT scan :
    - In acute interstitial pancreatitis, the pancreas is well perfused and uniformly enhanced by the intravascular contrast agent.
    - If necrosis is present, the areas of devitalized tissue are not perfused and are not enhanced.
- Findings of pancreatic infection :
    - Air bubbles in the pancreatic and peripancreatic region evidence
- CT-guided percutaneous aspiration, staining, and culture of the obtained fluid:
    - May help to distinguish sterile pancreatitis from pancreatic infection When fever, elevated WBCs, and clinical toxicity are associated with CT scan evidence of fluid collections or necrotizing pancreatitis
    - When infection is suspected or proved, surgical debridement may be lifesaving

3- ERCP

- Contraindicated except when an impacted common bile duct stone may be the cause of the pancreatitis
- Endoscopic sphincterotomy: may be immediately therapeutic.
- ERCP is also useful in diagnosis of :
    - Pancreas divisum
    - Annular pancreas
    - Pancreatic cancer
    - Periampullary, ampullary, and pancreatic ductal abnormalities
    - Communication of the pancreatic duct with pseudocysts.

Causes of Hyperamylasemia

Pancreatic trauma	Ruptured ectopic pregnancy
Pancreatitis	Ruptured or dissecting aortic aneurysm
Pancreatic pseudocyst	Splenic rupture
Pancreatic abscess	Renal insufficiency
Pancreatic cancer	Diabetic ketoacidosis

Biliary tract disease	Burns
Acute cholecystitis	Salivary gland disease
Common bile duct obstruction	Mumps
Perforated or penetrating peptic ulcer	Carcinoma
Intestinal obstruction	Lung
Intestinal ischemia or infarction	Esophagus
Peritonitis	Ovary
Acute appendicitis	Macroamylasemia

Differential diagnosis

1- It may be difficult to distinguish between acute cholecystitis, ascending cholangitis, and pancreatitis, because they may present with similarly elevated **serum amylase and abnormal liver tests**.

2- **U/S and HIDA** scans may be helpful in differentiating between these diseases

Acute cholecystitis	Mesenteric ischemia/infarction
Biliary colic due to choledocholithiasis	Vasculitis
Ascending cholangitis	Dissecting aortic aneurysm
Perforated viscus	Myocardial infarction
Penetrating peptic ulcer	Pneumonia
Alcoholic hepatitis	Renal colic
Viral hepatitis	Acute appendicitis
Acute intestinal obstruction	Diabetic ketoacidosis

Complications

1- **Pancreatic**

- Phlegmon
- Abscess
- Pseudocyst

2- **Nonpancreatic**

- Inflammatory involvement of contiguous organs

- Obstructive jaundice
- Pancreatic ascites
- Intraperitoneal hemorrhage
- Thrombosis of splenic vein
- Bowel infarction
- Fat necrosis of peritoneum and retroperitoneum
- Gastrointestinal bleeding

3- Metabolic

- Hypocalcemia
- Hyperlipidemia
- Hyperglycemia
- Diabetes ketoacidosis
- Nonketotic diabetic coma
- Pancreatic encephalopathy

4- Cardiovascular

- Cardiogenic shock
- Increased cardiac index
- Decreased systemic vascular resistance

5- Pulmonary

- Hypoxemia
- Pleural effusions
- Pulmonary infiltrates, atelectasis
- Adult respiratory distress syndrome

6- Renal

- Decreased glomerular filtration rate and renal plasma flow
- Acute tubular necrosis
- Acute renal failure

7- Hematologic

- Disseminated intravascular coagulation
- Thromboses
- Increased factor VII or fibrinogen

8- **Skin and musculoskeletal**

- Erythema nodosum-like lesions
- Angiopathic retinopathy
- Polyarthritis

Treatment

- In most patients (85%-90%) with acute pancreatitis, the disease is self-limited and resolves spontaneously.
- These patients are medically treated with supportive care with special attention given to:
  - Analgesia
  - Maintenance of normal intravascular volume
  - Frequent monitoring of vital signs
  - Treatment of possible complications of the disease.

1- **Meperidine (Demerol)**

- Dose : 50 - 100 mg every 4 - 6 hours IV or intramuscular (IM)
- Better tolerated than morphine sulfate (MS), which may induce spasm of the sphincter of Oddi.
- In cases of severe pain, MS may be necessary.

2- **IV electrolyte and colloid solutions should be given generously**

- 200-300 mL/L for the first 1-2 days to replace the fluid deficit.
- Fluid volume status determination may require Swan-Ganz catheter placement

3- **Nil by mouth + NGT suction**

- Putting the pancreas "at rest" by reducing pancreatic secretions → ↓ pancreatic inflammation
- NGT:
  - Decompresses the upper GIT and decrease gastric secretion and prevent gastric contents from entering the duodenum.
  - Used in patients with nausea, vomiting, and ileus.
  - It may not be necessary for the patient with mild disease

4- **No drugs effective in improving the course**

- Histamine-2 blockers or proton pump inhibitors are **no** more effective than nasogastric suction.
- Somatostatin or its analog octreotide may be beneficial by reducing pancreatic enzyme secretion
- Platelet activating factor antagonist (Lexipafant)
- Protease inhibitor and kallikreinin inactivator e.g. aprotinin (Trasylol vials)

5- Prophylactic antibiotics

- Not recommended in interstitial pancreatitis.
- Recommended in:
  - Possible secondary infection of the injured pancreatic tissue (phlegmon, pseudocyst, and abscess)
  - Obstructed biliary tract which may lead to ascending cholangitis
  - Necrotizing pancreatitis

6- Nutritional support

- As the inflammation subsides, small feedings of a diet high in carbohydrate but low in protein and fat may be initiated.
- It is important to advance the diet slowly.
- In patients who cannot receive feedings orally, parenteral nutritional support including intralipids should be instituted after the first few days.
- In some studies intragastric or intrajejunal feedings have shown decreased rate of infectious complications and should be preferred.

7- Patients with fulminant pancreatitis

- These patients have very large fluid requirements.
- Most patients may require mechanical respiratory support.
- Hypocalcemia and hypomagnesemia should be promptly treated with IV replacement.
- Patients may require dialysis.

8- Surgery

- Emergency laparotomy:
  - In patients with a deteriorating clinical condition

    - Performed to drain the necrotic pancreas and peripancreatic spaces
- Subtotal pancreatectomy and a procedure to decompress the biliary tract: advocated by some surgeons
- CT-guided percutaneous aspiration of the necrotic pancreas:
    - Alternatively, in clinically deteriorating patients with necrotizing pancreatitis may be done
    - Gram's stain and culture should be performed on the aspirated material.
    - Positive bacterial findings necessitate surgical debridement.
- Vigorous percutaneous drainage with multiple large tubes :
    - In selected cases of infected necrosis, have been successful in either delaying surgery until the patient is a better surgical candidate or eliminating the need for surgery.
- Endoscopic drainage :
    - In selected patients with organized infected necrosis
    - Imipenem and/or other antibiotics covering gut pathogens should be given.
    - In sterile necrosis, nonoperative medical management for the first 3 - 4 weeks is recommended.
- Endoscopic sphincterotomy: for common bile duct stones

Pancreatic pseudocysts

Definition

1- Are collections of **necrotic tissue, pancreatic juice, blood and fat** that develop in or near the pancreas over a period of 1 - 4 weeks after the onset of severe episode of acute pancreatitis

Characters

1- They do not have a true capsule with an epithelial lining. A connection may be present to a disrupted pancreatic duct.
2- Most pseudocysts (90%) are **solitary lesions** located in the body or tail of the pancreas.
3- The main symptom is **abdominal pain**.
4- **Persistence of an elevated serum amylase** level for more than a week after the onset of pancreatitis may signal the formation of a pseudocyst.
5- **Other causes** of pancreatic pseudocyst include:
   - Abdominal blunt trauma with disruption of a pancreatic duct
   - Inadvertent surgical ductal trauma
   - Chronic pancreatitis
   - Neoplastic cysts, such as cystadenoma or cystadenoma-carcinoma, account for 10% of cystic pancreatic masses.

Diagnostic studies

1- **Abdominal US and CT scans** are the best imaging techniques used in the diagnosis of pancreatic pseudocysts. Serial scans help in following the size and course of the cysts.
2- **ERCP** may be required to assess the possible connection of the pseudocyst with the pancreatic duct.

Treatment

1- Most pseudocysts tend to **resolve spontaneously** as the inflammation subsides.
2- If the pseudocyst is large or if there is a communication between the pseudocyst and a ruptured pancreatic duct with continued secretion of pancreatic juices into the enclosed space, the pseudocyst **may not resolve**
3- Symptomatic pseudocysts require **decompression** by:
   - Surgery or
   - Percutaneous catheter drainage or
   - Endoscopic techniques.
4- **Endoscopic and radiologic methods** should be reserved for those institutions with extensive experience in these techniques

Complications

1- **Infection**

- Patients with a pancreatic pseudocyst who have pain, fever, and leukocytosis need to be evaluated for infection.
- Percutaneous aspiration under US or CT guidance with Gram's stain and culture of the aspirate helps in confirming the diagnosis.
- Infected pseudocyst or abscess should be drained externally.

2- **Perforation**

- Rupture or leak of a pseudocyst into the peritoneal cavity or retroperitoneum may result in shock and requires emergency surgery.
- The mortality from this complication is very high.

3- **Hemorrhage**

- A pseudocyst may erode into a viscus (e.g., stomach, small or large bowel) or a blood vessel with subsequent hemorrhage.
- Angiography is often necessary prior to surgery for proper diagnosis of this complication.

Pancreatic cancer

Pathogenesis

1- **Age** → 60 - 80 yr

2- **Sex** → It is more common in men than in women (1.3:1)

3- **Predisposing factors**

- Smoking
- Diets rich in fat, red meat, or both
- History of peptic ulcer surgery (partial gastrectomy); cholecystectomy, possibly by increasing cholecystokinin (CCK) secretion
- Chronic pancreatitis (mostly hereditary and tropical types)
- Association:
  - Hereditary nonpolyposis colorectal cancer
  - Ataxia-telangiectasia
  - Peutz-Jeger syndrome

    - Familial breast cancer; familial atypical multiple mole melanoma
- Prolonged exposure to the gasoline derivatives 2-naphthylamine and benzidine and metal dusts.
- There is no conclusive evidence that drinking alcohol is related to the development of pancreatic cancer.
- Diets rich in fruits and vegetables, carotenoids, and selenium are probably protective (high fiber and vitamin C).

4- Pathology

- Site → 70% located in the head of pancreas & the remainder is in the body and the tail of the gland or are multifocal or diffusely infiltrate the gland
- Gross → dense, fibrotic mass in the pancreas associated with a desmoplastic reaction
- Microscopic → 90% adenocarcinoma arising from the duct epithelium
- By itself, the tumor may not cause symptoms. However, because the pancreas, which is a retroperitoneal organ without a mesentery, lies close to the porta hepatis, common bile duct, duodenum, stomach, and colon, the tumor mass may impinge on or penetrate into any of these structures and cause symptoms
- Spread :
    - Invades nerves and nervous plexuses, esp. in the celiac and mesenteric areas
    - The most common sites of extralymphatic metastasis are the liver, peritoneum, lungs, intestines, adrenals, kidneys, bones, and the diaphragm

Clinical presentation

1- **The early symptoms** → vague and nonspecific

2- An insidious weight loss with anorexia and nausea, accompanied by upper abdominal pain radiating to the back → is **the most common presentation**.

3- **Jaundice :**

- Initially in > 90% of the patients

  - Common bile duct obstruction by a tumor in the head of the pancreas may result in jaundice while the mass is still small (painless jaundice).
  - Tumors located in the body and tail of the organ may result in jaundice in later stages either by extension or due to metastasis to the porta hepatis or the liver parenchyma.

4- **DM or glucose intolerance**
  - In Up to 70% of the patients
  - The decreased or delayed insulin secretion is thought to arise from loss of B cells due to the desmoplastic reaction of the tumor

5- **Migratory thrombophlebitis (Trousseau's sign):**
  - May be a mode of presentation, but not specific for pancreatic cancer.
  - It may occur with other malignancies such as carcinomas of the stomach, colon, ovary, and lung.

6- **A minority of the patients** may also present with a picture of acute pancreatitis, cholangitis, gastrointestinal bleeding, polyarthritis, and skin nodules due to fat necrosis

7- Diarrhea, malabsorption, depression are common

8- Palpable gallbladder, epigastric mass, and nodular liver if **metastases** may be present

9- **Courvoisier's sign** → dilatation of gall bladder may occur with cancer head of the pancreas

10- **Warning signs for early diagnosis.**
  - Recent upper abdominal or back pain consistent with retroperitoneal lesion.
  - Recent upper abdominal pain or discomfort with negative gastrointestinal investigations.
  - Jaundice ± pruritus.
  - Weight loss > 5% of normal body weight.
  - Unexplained acute pancreatitis.
  - Unexplained onset of diabetes mellitus.

Differential diagnosis

1. A variety of **malignant and benign disorders** of other organs may present with features similar to pancreatic cancer.
2. Pancreatic cancer **may coexist in a patient with a common benign disorder** such as gallstones or peptic or diverticular disease, and normal contrast studies of the gastrointestinal tract, serum chemistries, and hemogram do not rule out the presence of pancreatic cancer, especially if the tumor is small.

Investigations

1. **Laboratory tests:**
    - If there is involvement of the liver or the biliary tract, this will be reflected in the serum chemistries.
    - The serum amylase and lipase in most instances are normal.
    - A subgroup of patients has elevated blood glucose levels.
2. **Tumor markers**
    - CEA, CA 19-9, alpha-fetoprotein, pancreatic oncofetal antigens, pancreatic ribonuclease, and galactosyl transferase isoenzyme II.
    - CA 19-9:
        - The most widely used
        - It is not specific for pancreatic cancer (↑in the bile ducts and colon tumors).
        - Not reliable for use in screening because levels are frequently normal in the early stages of pancreatic cancer
        - High levels may help differentiate between benign diseases of the pancreas and pancreatic cancer.
        - Useful marker for follow-up surveillance, as when the pancreatic cancer is completely resected, levels fall
    - The ratio of testosterone to dihydrotestosterone is < 5 (normal is 10):
        - In more than 70% of men with pancreatic cancer
        - Presumably because of increased conversion of testosterone by the pancreatic tumor.

    - This ratio may be more sensitive than CA 19-9 in detecting smaller pancreatic cancers and more specific than the other markers.

3- U/S and CT with contrast

- The most sensitive and specific for pancreatic disease.
- Findings:
    - Both demonstrate enlargement of the gland, alteration in contour or consistency of the gland
    - The presence of masses, and biliary or pancreatic duct dilatation.
    - CT scans may also delineate peripancreatic nodal enlargement as well as invasion of other organs and vessels.
- US and CT are complementary in imaging the pancreas:
    - The lesions in the head of the pancreas are seen well by US, whereas those in the body and tail are detected better by CT scan.
    - However, small lesions, especially in the body or tail, may be missed by both techniques.
    - Helical thin section CT scan with IV contrast and CT angiography (CTA) increase the diagnostic yield.

4- Contrast enhanced MRI using IV gadolinium-DPTA

- Useful for detecting small pancreatic tumors.
- Ductal size is evaluated by MRCP.
- MR arteriography (MRA) has obviated the need for angiography and improves the examination of the pancreas for tumor.
- Fat-saturation MRI is especially valuable in looking for suspected tumors in a pancreas that is not enlarged.

5- ERCP

- Findings:
    - Pancreatic duct stenosis or obstruction caused by the tumor.
    - An accompanying cholangiogram may further delineate abnormalities along the course of the common bile duct.
    - It can also visualize and differentiate ampullary and duodenal carcinomas.

    - Biopsies of periampullary tissue and cytologic examination of aspirated pancreatic juice may increase the diagnostic yield further.
- Indicated: if an abnormality is noted on the US or CT scan or if an abnormality is suspected but cannot be demonstrated by these methods.
- ERCP may be used to place stents in the obstructed biliary and pancreatic ducts to relieve obstruction and palliate patients with unresectable tumors.

6- EUS

- Detect too small lesions not seen by CT or transabdominal US.
- Detect associated lymph nodes and vascular involvement accurately
- Staging of pancreatic cancer with EUS may become routine before selection of therapy.
- EUS guided fine-needle aspiration allows cytologic evaluation.

7- Angiography

- Celiac and superior mesenteric angiography with selective cannulation of the pancreatic vessels may provide a sensitive diagnostic tool.
- Best used to determine resectability of the tumor before surgery.
- Arterial encasement, venous occlusion, and tumor vascularity can be visualized
- If a tumor is resectable, the arterial blood supply and anatomic variations of the foregut vasculature can be delineated by angiography to help in the planning of surgery.

8- Cytologic diagnosis

- Direct percutaneous fine-needle aspiration can be performed with US, CT, EUS, or angiographic guidance.
- Allow differentiation of lymphoma or endocrine tumors from adenocarcinoma or chronic pancreatitis without surgery
- Drawbacks:
    - Negative result cannot exclude the presence of a malignant tumor, especially if the tumor is small
    - Tumor seeding with possible peritoneal spread of the tumor.

9- Percutaneous transhepatic cholangiogram (PTC)

- **M**ay visualize the common bile duct and the site of its obstruction in patients with obstructive jaundice with dilated bile ducts
- A drainage catheter may then be introduced percutaneously for biliary decompression.

10- Laparoscopy

- Detect too small distant metastasis not detected by CT (The most common sites of distant metastasis from pancreatic cancer are the liver, the peritoneum, and the omentum)

Staging

1- Stage I: confined to pancreas alone
2- Stage II: involving only neighboring structures
3- Stage III: involving regional lymph nodes
4- Stage IV: including liver and other distant spread

Treatment

1- Definitive surgery:

- Only 5% - 22% had a resectable tumor at the time of diagnosis.
- Operation:
  - Pancreaticoduodenectomy (the Whipple's operation) or a modification of this procedure.
- Principle of the Whipple's operation:
  - En bloc removal of the duodenum, a variable portion of the distal stomach, and the jejunum, gallbladder, common bile duct, and regional lymph nodes
  - Followed by pancreaticojejunostomy and gastrojejunostomy.
  - Vagotomy should be performed if > 60% of the stomach is removed.
  - Total pancreatectomy does not offer better results; however, it produces exocrine insufficiency and brittle diabetes, which is difficult to manage.
- A less extensive operation:

    - That preserves the pylorus and avoids postgastrectomy symptoms is being used with no apparent compromise of long-term survival.
    - In most of these patients, the cancer is at the head of the pancreas.
- The 5-year survival of patients who undergo pancreatic resection is 17% - 24% in large centers.
- Better prognosis occur in:
    - Smaller tumors (<2 cm in diameter)
    - Patients without lymph node metastases or major vessel involvement
    - Those with no residual tumor. In such patients, the 5-year survival may be as high as 57%.

2- Palliative surgery

- Biliary obstruction due to unresectable cancer head:
    - A bypass procedure may be performed to decompress the biliary tract.
    - Cholecystojejunostomy, choledochojejunostomy, or hepatojejunostomy may be done, depending on the site of obstruction.
    - Because approximately one third of the patients with ductal adenocarcinoma of the head of the pancreas eventually have duodenal obstruction, a gastrojejunostomy may be performed at the same time to spare the patient a second laparotomy.
    - In debilitated patients, a percutaneous or endoscopically placed biliary stent may decompress the biliary tract, with the following complications; stent occlusion, recurrent jaundice, and infection. However, the new, expandable metal stents seem to avoid these complications.
    - Duodenal obstruction can be treated only by surgery.
- Cancer of the body or tail of the pancreas:
    - Diagnosed at a late stage.

        - True cut biopsy is important to to rule out endocrine cancer in because endocrine tumors are much more amenable to treatment and have a much better prognosis.
    - Abdominal and back pain:
        - The injection of phenol or absolute alcohol around the celiac plexus for the relief of pain is helpful in some patients.
        - Done during laparotomy or percutaneously.
        - Narcotics and radiotherapy may also be used.

3- **Chemotherapy**

- Most patients with stages I and II and some with stage III disease who are reasonable surgical candidates should be treated surgically.
- However, some patients with stages III and IV disease have been treated with single- or multiple-agent chemotherapy with variable results.
- The drugs used are 5-fluorouracil, mitomycin, carmustine, lomustine, methyl CCNU, streptozotocin, and Gematabine.

4- **Radiation therapy**

- The combination of radiation therapy (4,000-6,000 rad) with chemotherapy (using 5-FU) has been found to result in enhanced radiation therapeutic efficiency.
- Newer radiation techniques using iodine 125 directly implanted into the tumor tissue and neutron beam radiation show promise in the treatment of unresectable cancer of the pancreas.

5- **Intraoperative radiation therapy**

- A single dose of 20 Gy is delivered to the surgically exposed cancer by an electron beam through a field-limiting cone.
- Unfortunately, in 30% of these patients unavoidable irradiation of the duodenum may result in bleeding, obstruction, and perforation.
- In most patients, therefore, protective gastrojejunostomy is performed at the same time as the intraoperative radiation.

6- Intensive **supportive and nutritional therapy**, either enteral or parenteral, as indicated

APPROACH TO SPECIFIC SYMPTOMS

Dysphagia

Definitions

1- **Dysphagia :** difficulty in swallowing or the sensation of an obstruction in the passage of food (semisolid, solid and/or liquid) anywhere from the mouth to the stomach

2- **Odynophagia :** pain during swallowing (dysphagia and odynophagia may coexist in the same patient)

3- **Globus :** constant sensation of a lump or fullness in throat without difficulty swallowing

4- **Aphagia :** inability to swallow
    - Can result when a food bolus gets impacted in the esophagus, thus blocking passage of any further boluses
    - Can also result from pharyngeal muscle paralysis from lower cranial nerve involvement

5- **Xerostomia :** dryness of the mouth from ↓ salivation, which can cause trouble initiating a swallow because of poor lubrication of the food bolus, causes include
    - Sjogren's syndrome
    - Radiation to head and neck
    - Medication side effects

Incidence → 16-22% of individuals > 50 yrs

Esophageal dysphagia

Etiology

1- Occurs when there is a disruption in the **esophageal phase of swallowing**

2- Arise commonly from **structural defects** within the body of the esophagus, LES or gastric cardia

3- May be caused by diseases of esophageal smoth muscle, the autonomic nervous system and/or mucosa of the esophagus

Causes of esophageal dysphagia	
Structural causes (more common)	**Motility disorders**
Benign stricture Esophageal cancer Schatzki ring Esophageal webs Foreign bodies Extrinsic (vascular, cervical osteoarthritis, adenopathy)	Achalasia Scleroderma Hypertensive lower esophageal sphincter Diffuse esophageal spasm Chagas' disease Nutcracker esophagus
N.B. Eosinophilic esophagitis is recently becoming a recognized cause of dysphagia esp. in young adults	

Clinical presentation

1- **C/O**
  - Food sticking in the throat or the chest
  - The sensation of dysphagia may be referred to the sternal notch despite the fact that the point of obstruction may be in the distal esophagus

2- **Timing** → few seconds after swallowing

3- **Associated symptoms** may be
  - Regurgitation soon after swallowing which may taste similar to food just eaten and not sour or bitter (which implicates retrograde transit from the stomach, as in reflux disease or emesis)
  - Or retrosternal chest pain

4- **In structural causes** → dysphagia initially to solid foods but may later include liquids as well

5- **In neuromuscular disorders** → dysphagia to both solids and liquids start from the onset of symptoms

6- **In eosinophilic esophagitis** → dysphagia can present with intermittent food bolus impactions

Diagnostic testing

1- Upper endoscopy

- The 1st test of choice for evaluation of esophageal dysphagia
- Values
  - Allows for direct visualization of the esophagus
  - Tissue biopsy can be taken
  - Structural narrowing can be dilated if found

2- Barium swallow (esophagogram)

- Indications
  - Suspicion of subtle strictures or narrowings or
  - If road mapping of a tight or complicated stricture is desired before endoscopic evaluation
- Values
  - Detect structural abnormalities such as tumors, webs and rings
  - Determine the length and degree of narrowing of a structural lesion
  - Aids in the detection of subtle abnormalities
  - Detect motility disorders such as achalasia, diffuse esophageal spasm and scleroderma [but manometry is typically required for definitive diagnosis]

3- Esophageal manometry

- Indications
  - If no structural or obstructive lesion is identified on upper endoscopy or barium swallow
- Values → definitive diagnosis of motility disorders
- High resolution manometry → improve the sensitivity of diagnosis of LES relaxation abnormalities

Oropharyngeal dysphagia

Etiology

1- Occurs when there is a disruption in the **oral or pharyngeal phases** of swallowing

2- Most commonly caused by **neurogenic** (lesions of the swallowing center, cranial nerves) and **myogenic** disorders of oropharyngeal muscles, lesions of the mucosa or teeth and rarely as a result of oropharyngeal or base of skull tumors

3- Arise from disorders that affect the function of the oropharynx, larynx and UES

Causes of oropharyngeal dysphagia	
Neuromuscular disorders (more common)	**Structural lesions**
Cerebrovascular accident Parkinson's disease Amyotrophic lateral sclerosis Poliomyelitis Polymyositis Myasthenia gravis Brain tumors Hypothyroidism Abnormal upper esoph. sphincter relaxation	Neoplasm Inflammation (pharyngitis, radiation) Plummer-Vinson syndrome Cervical hyperostosis Thyromegaly Lymphadenopathy Prior oropharyngeal surgery Zenker's diverticulum

Clinical presentation

1- **C/O** → difficulty initiating a swallow or coughing, choking, drooling and nasal regurgitation after swallowing

2- **Timing** → typically within 1 second of initiating a swallow

3- **Type of foods** → difficulty occurs with solids and/or liquids

4- **Physical examination** may show

- Evidence of neurologic dysfunction in the lower cranial nerves
- Generalized muscle weakness or dystrophy

Diagnostic testing

1- **Careful neurologic examination** → is the 1st step in evaluation

2- Modified barium swallow/videofluoroscopy

- Principle → the patient swallows barium of various consistencies, such as thin liquids, thick liquids and barium cookies or a cracker

- Values
  - Identify abnormalities of the oropharyngeal phases
  - May direct therapy (patients may tolerate certain consistencies better than others)

3- Direct laryngoscopy

- Indicated if structural lesions are identified for further evaluation

4- **High resolution manometry** (recently with 3D)

- Evaluate the pharyngeal muscle and upper esophageal sphincter function

History in both types [important in determination of the cause of dysphagia; esophageal or oropharyngeal]

1- Duration of symptoms and acuity of onset

2- Intermittent or progressive **course**

3- **Aspiration symptoms** (cough or choking episodes while swallowing)

4- Symptoms of lower cranial nerve dysfunction, such as
  - Regurgitation through the nose
  - Drooling or food spilling from the corners of the mouth

5- **Associated symptoms** like heartburn or chest pain

6- Weight loss

7- **Food items** that typically cause difficulty (esp. solids, liquids or both)

8- The patients can be asked to describe **where** they feel the disturbance is located

9- **History of medications** → causing direct esophageal mucosal injury
  - Tetracycline, doxycycline
  - Clindamycin

10- **History of atopic disorders and asthma** → eosinophilic esophagitis

11-History of radiation to head and neck

Physical examination in both types

1- **General examination** with attention to
  - Examination of oral cavity, head and neck
  - Nutritional status (including body weight)

2- **Neurological examination** with attention to

  - Resting tremors
  - Cranial nerves
  - Muscle strength

3- If **easy fatigability** present → observe the patient while performing a repetitive task e.g. blinking or counting aloud

4- Observe the **gait and balance** → to check for parkinson's disease

5- Examine the **skin** esp. palms and soles → for thickening or texture changes

6- Evaluate the **neck** → for thyromegaly or other mass

7- Inspect the **muscles** for wasting and fasciculations and palpate for tenderness → to detect an underlying motor neuron disease

Complications

1- Aspiration

2- Pneumonia

3- Dehydration

4- Weight loss and malnutrition → with prolonged dysphagia

5- Esophageal perforation → rarely with aggressive dilatation of strictures

Treatment

1- Lifestyle/risk modification

- Diet
  - Change the patient diet or the consistency to aid swallowing
  - A modified barium swallow may help identify certain consistencies that can be swallowed better than others
  - There is particularly relevant in oropharyngeal dysphagia from neuromuscular disease and in esophageal dysphagia where there is residual dysphagia after treatment
- Activity
  - A speech-language pathologist can help the patient to learn different exercises and head and neck positions that may aid swallowing

2- Medications

- Infectious esophagitis

- Eosinophilic esophagitis
- Dysphagia caused by acid reflux disease

3- Nonpharmacologic therapy for esophageal dysphagia

- Treatment of the underlying disorder
- Strictures → endoscopic dilatation
- Rings and webs→ endoscopic disruption
- Obstructing tumors → surgery, dilatation or placement of endoscopic stent
- Large obstructing tumors not amenable to dilatation or stent placement → Gastrostomy tube placement
- Acalasia → surgical myotomy and pneumatic balloon dilatation
- Disorders of LES relaxation as acalasia → botulinum toxin injection into the LES via endoscopy
- Eosinophilic esophagitis → topical steroids + exclusion diets; intermittent dilatation of dominant strictures may be sometimes necessary
- Empiric endoscopic dilatation with a large caliber dilator → often performed when routine investigations fail to reveal a definitive etiology

4- Nonpharmacologic therapy for oropharyngeal dysphagia

- Treatment of the underlying disorder when possible
- However, many patients have irreversible or progressive neurologic disease which can lead to worsening the dysphagia
- Consultation with a speech therapist is often helpful in modifying eating behaviors and food consistency
- In some patients where there is no significant improvement
  - NGT feeding
  - Percutaneous gastrostomy or jejunostomy tubes
- Excessive drooling or secretions can be suppressed by
  - Anticholinergic drugs or
  - Tricyclic antidepressants

Functional dysphagia

1- **Definition:** disorder characterized by sensation of abnormal bolus transit through the esophagus in the absence of structural lesions, GERD and histopathology based esophageal motility disorders

2- **Etiology :** ↑ perception of esophageal sensation, sometimes triggered by noxious stimuli like GERD

3- **Clinically :** sense of solid and/or liquid foods sticking, lodging or passing through esophagus

4- Treatment :

- Treatment of associated reflux disease
- Low dose tricyclic antidepressants may be of value

Constipation

Definition

1- Infrequent stools, difficult stool passage or both

2- Associated symptoms include → passage of hard stools, straining, unproductive urges and the sensation of incomplete evacuation

Classification

1- Primary versus secondary

- 2ry constipation occurs as a side effect of various conditions and medications

2- Acute versus chronic

Risk factors

1- Age → > 50% of the elderly

2- Sex → females > males

3- Physical inactivity

4- Malnutrition and restricted diets

5- Polypharmacy

6- Recent abdominal or pelvic surgery
7- Known comorbid conditions
8- Travel

Etiology of 1ry constipation

1- **Normal transit constipation** → patients have symptoms without evidence of delayed colonic transit
2- **Slow transit constipation** → idiopathic entity with delayed transit from the proximal to distal colon
3- **Pelvic floor dyssynergia** → occurs when the puborectalis and anal sphincter muscles fail to relax or paradoxically contract with attempted defecation ; colonic transit to the rectum can be normal in this disorder
4- **Constipation predominant irritable bowel syndrome** → considered if the patient has < 25% loose or watery stools or ≥ 25% hard or lumpy stools

N.B. considerable overlap between these categories is noted

Differential diagnosis of constipation (causes)	
Endocrine	DM, pregnancy, hypothyroidism, hyperparathyroidism, pheochromocytoma
Metabolic	Chronic kidney disease, hypercalcemia, hypokalemia, hypomagnesemia, porphyria, heavy metal poisoning
Neurologic	Hirschsprung's disease, Chagas' disease, parkinson's disease, spinal cord injuries or tumors, autonomic neuropathy, intestinal pseudoobstruction, stroke, multiple sclerosis, dementia
Myopathies	Scleroderma, amyloidosis, myotonic dystrophy
Structural	Colon cancer, stricture, external compression, rectocele, fissure, hemorrhoids
Drugs	Analgesics, tricyclic antidepressants, anticholinergics, antihistamines, antipsychotics, antiparkinsonian agents, antidiarrheals, antacids, anticonvulsants, calcium channel blockers, diuretics, cation-containing agents (e.g. iron, bismuth), bile acid resins
Others	Irritable bowel syndrome, anal spasm, rectal prolapse, depression, low fiber diet, sedentary lifestyle, slow transit constipation, pelvic floor dysfunction

N.B in elderly, the etiology is often multifactorial and can include comorbid illness, medications and decreased mobility. Care should be taken to monitor hydration and electrolytes closely esp. in those with renal disease

Rome 111 diagnostic criteria for functional constipation
At least 3 mo (with symptom onset at least 6 mo prior to diagnosis) ot ≥ 2 of the following: - Straining with ≥ 25% of defecations - Lumpy or hard stools with ≥ 25% of defecations - Sensation of incomplete evacuation with ≥ 25% of defecations - Sensation of anorectal obstruction or blockage with ≥ 25% of defecations - Manual maneuvers to facilitate ≥ 25% of defecations - < 3 defecations per week
Loose stools are absent without use of laxatives
Insufficient criteria for the diagnosis of constipation predominant IBS

History

1- **Well performed defecation history**

- Infrequent stools, hard stools, sense of incomplete evacuation
- Straining, need for digital disimpaction
- Associated abdominal pain

2- **Onset and duration** → e.g. lifelong abdominal discomfort may suggest overlap with irritable bowel syndrome

3- **The Bristol stool scale** → the best descriptor of stool form and consistency and a useful guide to intestinal transit time

Type 1	Separate hard lumps, like nuts (hard to pass)
Type 2	Sausage shaped but lumpy
Type 3	Like a sausage but with cracks on its surface
Type 4	Like a sausage or snake, smooth and soft
Type 5	Soft blobs with clear cut edges (passed easily)
Type 6	Fluffy pieces with ragged edges, a mushy stool
Type 7	Watery, no solid pieces. Entirely liquid

4- **Symptoms assessment**

- Cold intolerance and weight gain → hypothyroidism
- Triad of kidney stones, confusion and constipation → hypercalcemia
- Current diuretic use or vomiting → hypokalemia and ileus
- Esophageal dysmotility with constipation → systemic sclerosis

- History of weight loss, bloody stools, family history of cancer colon, prior screening colonoscopy and obstructive symptoms (late) → cancer colon

5- **Careful medication history**

Physical examination

1- **General examination e.g.**

- Thyroid goiter → suggest endocrinal etiology
- Peripheral neuropathy → suggest neurological etiology

2- **Abdominal examination**

- Inspection → signs of previous surgery
- Palpation → distention, masses or retained stool
- Auscultation → bowel sounds (presence and frequency)

3- **Perineal and rectal examination**

- Inspection → internal hemorrhoids, fissures or masses
- Perineal sensation and the anal wink reflex
- Digital examination
  - Anorectal neuromuscular function → can be evaluated by checking the sphincter tone both at rest and with squeeze
  - Gaping of the anal canal on immediate withdrawal of the finger → may suggest external anal sphincter denervation
  - Asking the patient to bear down → may reveal rectal prolapse, rectocele or paradoxical contraction
  - Significant pain on digital examination → can imply a fissure or ulceration

Diagnostic teasting

1- **Laboratory tests**

- CBC
- Glucose and calcium
- TSH
- Occult blood in stool

- Specific testing for endocrinopathies, metabolic disorders or collagen vascular disorders only done if high suspicion exists

2- Imaging

- Plain abdominal X-ray
  - Detect ileus, obstruction, megacolon or stool retention
- Barium radiography
  - Performed if plain X-ray suggestive of megacolon, megarectum or structural disease with luminal narrowing
- Defecography and dynamic MRI
  - Helpful when previous studies are inconclusive

3- Diagnostic procedures

- Flexible sigmoidoscopy and colonoscopy
  - Indicated for new onset constipation of unclear etiology esp. if age > 50, esp. in the presence of warning signs such as weight loss, anemia, bloody stools, family history of colon cancer or hemoccult positive stools [to exclude colorectal cancer]
  - Hemorrhoids, fissures and stercoral ulcers can be detected
  - Melanosis coli: a brownish black discoloration of the bowel mucosa is sometimes seen in the presence of chronic anthraquinone laxative use
- Colonic transit studies
  - Can distinguish causes of primary constipation
  - One type involves ingestion of raio-opaque markers, with plain radiography performed 5 days later. If ≥ 6 markers are left scattered throughout the colon → slow transit is suggested & if those markers are confined to the rectosigmoid colon → there may be element of obstructive defecation
  - A new, wireless capsule technique called the smart pill can provide similar information while also assessing transit and PH in the stomach and small bowel
- Anorectal manometry

    - Provides an assessment of both pressure activity and sensation of the anorectum and its sphincters
    - These measures are carefully evaluated during rest, squeeze and bear down maneuvers
    - A ballon inflation test measures the patient's symptoms at various pressures. Finally, a ballon expulsion test can be performed to assess the patient's ability to expel a simulated bowel movement , typically within 2 minutes in normal subjects

Complications

1- Fecal impaction
2- Pudendal nerve damage
3- Fecal incontinence
4- Rectal prolapse
5- Stercoral ulcers with perforation or bleeding
6- Volvulus
7- Hemorrhoids and anal fissures

[Complications more frequent in elderly and nursing home residents]

Treatment

1- Lifestyle/Risk modification

- Proper fluid intake and exercise → could be beneficial

2- Principle of therapy

- Initial therapy involves use of dietary fiber supplementation and laxatives
- If this 1st line fails → assessment of colonic and/or anorectal function is appropriate before starting further medications

3- 1st line medications

- Fiber supplementation
    - Begin at 10 g/day and ↑ by 5 g/day each week to a total intake of 25 g/day
    - Adequate hydration is important during trials of increased fiber, as constipation can potentially worsen

    - Side effects include → bloating, abdominal distention and flatulence
- Osmotic laxatives
    - Drugs → lactulose, mixed electrolyte solutions (polyethylene glycol)
    - Action → ↑ fluid in the bowel lumen by osmosis
    - Side effects → electrolyte imbalance, dehydration and urge incontinence because of the fluid volume delivered to the rectum
- Saline laxatives
    - Drugs → magnesium citrate, phosphate and sulfate
    - Action → similar to osmotic laxatives
    - Side effects → dehydration, abdominal cramping and magnesium toxicity (avoid in renal dysfunction)
- Stimulant laxatives
    - The most frequently prescribed drugs
    - Drugs → senna and bisacodyl
    - Action → ↑ colonic motility. Anthraquinones additionally increase fluid and electrolyte content in the distal ileum and colon
    - Side effects → abdominal cramping, cathartic colon and melanosis coli (senna, cascara)
- Emollients
    - Mineral oils → penetrates the stool and softens it
    - Docusate salts → ↓ surface tension of stool, allowing more water through
    - Side effects → malabsorption of fat soluble vitamins and lipid pneumonia if aspirated
- Enemas
    - Use tape water, saline, mineral oil or Na phosphate to cause distal colonic distension and reflex evacuation of luminal contents
    - Side effects → mechanical trauma and damage to rectal mucosa with chronic use

4- **2nd line medications**

- 5-hydroxytryptamine-4 (5-HT4)
  - Action → receptor agonists have prokinetic effects
  - Older drugs as cisapride and regaserod, have been taken off the market due to potential cardiovascular side effects
  - Newer drugs such as prucalopride has been approved in Europe at a dose of 2 mg/day in adults and 1 mg/day in the elderly
- Lubiprostone
  - Action → CL channel activator that ↑ intestinal water secretion
  - Approved for use both in constipation predominant IBS and chronic constipation
  - Side effects → nausea
- Linaclotide
  - Action → guanylate cyclase C activator that leads to intestinal CL and HCO3 secretion [studies are ongoing]
- Mu-receptor antagonists
  - Methylnaltrexone → used to treat patients with opioid related constipation, promotes bowel movements without decreasing the pain relieving effects of narcotics
  - Alvimopan → used successfully in postoperative ileus

5- **Non-pharmacologic therapies**

- Biofeedback
  - A type of behavioral training that has shown benefit in defecatory disorders, both in improving symptoms and anorectal function
  - Patients are retrained to relax their pelvic floor muscles and restore normal anorectal synergy during defecation
  - This method appears to be beneficial primarily in those with outlet dysfunction
- Ritualization of bowel movement timing

6- **Surgery**

- Structural abnormalities that obstruct defecation as enterocele, rectocele, cystocele
- Refractory slow transit constipation or colonic inertia → sometimes need total colectomy with ileorectal anastomosis [pelvic floor dyssynergia must be excluded first]
- Stercoral ulcers with perforation → surgery
- Stercoral ulcers causing rectal bleeding → endoscopic therapy to achieve hemostasis

Fecal impaction

Diagnosis

1- Fecal impaction should always be **considered** in patients with chronic constipation regardless of whether presentation involves constipation or incontinence
2- Fecal impaction can lead to **incontinence** by invoking the rectoanal inhibitory reflex, that is the tendency for the internal anal sphincter to relax in the presence of stool in the rectum
3- A quick **digital rectal examination** can often detect stool in the rectum. However, fecal impaction sometimes occurs higher than the rectum and absence of stool in the rectum does not exclude the diagnosis
4- **Plain X-ray of the abdomen** → may reveal obstructive features and lack of rectal air

Treatment

1- **Manual disimpaction**
2- **Oil based enemas** (cottonseed enema, mineral oil enema) → may help soften the stool and ease evacuation
3- **Hypaque enemas** → may provide both diagnosis and therapy
4- **After disimpaction**, an effective oral laxative regimen ± rectal suppositories or enemas needs to be established

Diarrhea

Definitions

1. **Diarrhea**
   - ↑ In the fluidity, frequency, and volume of daily stool output.
   - The daily stool weight is usually increased over the normal average of 200 g due to an increase in the stool water above the normal content of 60% to 75%.
2. **Acute diarrhea** → duration < 2 -3 weeks
3. **Chronic diarrhea** → duration > 3 weeks in adults & > 4 weeks in infants
4. **Antibiotic associated diarrhea** → If diarrhea occurs in the setting of antibiotic therapy or after a course of antibiotics (also, pseudomembranous colitis due to C. difficile cytotoxin should be considered)

Pathophysiology [4 mechanisms]

1. **O**smotic diarrhea, in which there is increased amounts of poorly absorbable, osmotically active solutes in the gut lumen.
2. **S**ecretory diarrhea, in which there is, increased Cl^- and water secretion with or without inhibition of normal active Na^+ and water absorption.
3. **E**xudation of mucus, blood, and protein from sites of active inflammation into the bowel lumen.
4. **A**bnormal intestinal motility, with increased or decreased contact between luminal contents and mucosal surface.

Osmotic diarrhea

Causes

1. **Carbohydrate malabsorption**
   - Disaccharidase ↓ in the small intestinal mucosa
     - 1ry e.g. idiopathic lactase, sucrose-maltase ↓
     - 2ry e.g. after infectious GE and with mucosal inflammation
   - Ingestion of mannitol, sorbitol (diet candy, soda, chewing gum)
   - Lactulose therapy

2. **General malabsorption**
    - Sprue (idiopathic gluten enteropathy, tropical)
    - Postradiation and postischemic enteritis
3. **Ingestion of**
    - Sodium sulfate (Glauber's salt), sodium phosphate
    - Magnesium sulfate (Epsom salts), milk of magnesia
    - Magnesium containing antacids

Clinically

1. Osmotic diarrhea **stops** when the patient fasts.
2. The stool **osmolality** ($[Na^+]+[K^+]) \times 2$ (to account for anions) is < the osmolality of the stool fluid measured by freezing point depression.
3. This **osmotic anion gap** accounts for the presence of the poorly absorbable solutes in fecal fluid.
4. **Anion gaps > 50** are considered clinically significant.
5. **Stool pH** may be helpful in the diagnosis of osmotic diarrhea
    - Carbohydrates → acid pH
    - Milk of magnesia → alkaline pH
    - Poorly absorbable salts containing Mg^{2+} or $SO^2{}_4^-$ → a neutral pH

Secretory diarrhea

Clinically [5 features]

1. Stool **volume** → usually large (>1 L per day).
2. Stools **consistency** → watery
3. Stools **do not contain** pus or blood
4. **Diarrhea:**
    - Typically continues while the patient fasts for 24 - 48 hours.
    - However, secretory diarrhea from fatty acid malabsorption or from laxative abuse will stop when these agents are not ingested.
5. **The osmolarity of the stool** → is close to the osmolality of plasma, and there is no anion gap

Causes

- Diarrhea of 1 L or more per day results from secretion of fluid across the intestinal mucosa.
- In most cases, a pathophysiologic event causes small intestinal secretion by simultaneously stimulating active secretion and partial inhibition of intestinal absorption.
- Often, the intestinal mucosa is intact and has normal histologic findings.

1- Enterotoxins

- Vibrio cholera
- Escherichia coli
- Staphylococcus aureus
- Bacillus cereus

2- Hormonal secretagogues

- Vasoactive intestinal polypeptide (pancreatic cholera syndrome, secreting villous adenoma)
- Calcitonin (medullary carcinoma of thyroid)
- Serotonin (carcinoid)
- Prostaglandins, prostanoids (intestinal lymphoma, inflammatory bowel disease)

3- Gastric hypersecretion

- Zollinger-Ellison syndrome
- Short-bowel syndrome
- Systemic mastocytosis
- Basophilic leukemia

4- Laxatives

- Ricinoleic acid (castor oil)
- Bisacodyl
- Dioctyl sodium sulfosuccinate
- Aloe
- Senna
- Danthron
- Phenolphthalein

5- Bile salts

- Terminal ileal disease/resection
- Bile duct obstruction

6- **Fatty acids**

  - Pancreatic insufficiency
  - Small-intestine mucosal disease

Exudative diarrhea

Clinically

1- If the intestinal mucosa is inflamed and ulcerated, **mucus, blood, and pus** leak into the lumen and are discharged as stool.

2- This may also create an increased osmotic load.

3- **If a large surface area** of the bowel lumen is involved, absorption of ions, solutes, and water will also be impaired, and patients may have large-volume diarrhea.

4- Inflammation may generate **prostaglandins**, which stimulate secretion and may increase bowel motility, thus compounding the diarrhea.

Causes [the inflammation may be]

1- Idiopathic (e.g., Crohn's disease, ulcerative colitis)

2- Infectious (e.g., from invasive organisms or cytotoxins: Shigella, Salmonella, Campylobacter, Yersinia, tuberculosis, amebae, and Clostridium difficile)

3- Ischemic

4- Vasculitic

5- Due to radiation injury

6- Caused by abscess formation (e.g., diverticulitis, infected carcinoma)

Motility disturbances

1- **Increased motility of the small intestine**

  - Mechanism: decreased contact time of chyme with absorptive surfaces.
  - Type of diarrhea: secretory
  - Causes: hyperthyroidism, carcinoid, and postgastrectomy dumping syndrome are examples

2- **Decreased motility of the small intestine**

- Mechanism: colonization of the small intestine with colonic-type bacteria.
- Type of diarrhea: osmotic or secretory diarrhea.
- Causes: diabetes, hypothyroidism, scleroderma, amyloidosis, and postvagotomy states.

3- Increased colonic motility

- Mechanism: premature emptying of colonic contents
- Causes: major cause of diarrhea in the irritable bowel syndrome.

4- Anal sphincter dysfunction

- Fecal incontinence, which may be interpreted by the patient as diarrhea
- Causes: neuromuscular disease, inflammation, scarring, and postsurgical states

Causes of acute diarrhea

1- Small intestine

- Viral infections
  - Rota virus
  - Norwalk virus
  - Enteric adenovirus
- Bacterial infections
  - Vibrio cholerae
  - Toxigenic E. coli
- Food poisoning
  - S. aureus
  - Bacillus cereus
  - C. perfringens
  - C. botulinum
- Parasitic infections
  - Giardia lamblia
  - Cryptosporidium

2- Colon

- Bacterial infections
  - Salmonella
  - Shigella

        - Campylobacter
        - Yersinia enterocolitica
        - Invasive E.coli
        - E .coli O157:H7
        - S .aureus (toxin)
        - Vibrio parahaemolyticus (toxin)
        - Clostridium difficile (toxin)
    - Parasitic infections
        - Entamoeba histolytica

3- Drugs

- Laxatives
- Sorbitol
- Antacids (Mg, Ca salts)
- Lactulose
- Colchicine
- Quinidine
- Diuretics
- Digitalis
- Propranolol
- Theophylline
- Aspirin
- NSAIDs
- Chemotherapeutic agents
- Antibiotics
- Cholinergic agents
- Heavy metals (Hg, Pb)

4- Miscellaneous

- Fecal impaction
- Diverticulitis
- Ischemic bowel disease

5- Traveler's diarrhea [during or just after traveling commonly infectious]

- Enterotoxigenic E. coli
- Salmonella
- Giardia and amebae

6- Homosexual individuals

- Amebiasis and giardiasis
- Shigellosis

- Rectal syphilis and rectal gonorrhea
- Lymphogranuloma venereum (C. trachomatis)
- Herpes simplex infection of the rectum and peri- anal area

7- HIV → see infection for details

- CMV
- Cryptosporidium
- Candida

8- Liver disease or malignancy → Plesiomonas species

Causes of bloody diarrhea

1. **C**ampylobacter
2. **E** .coli (enteropathogenic and invasive)
3. **S**higella
4. **S**almonella
5. **E** .coli O157:H7
6. **Y**ersinia
7. **V**ibrio parahaemolyticus
8. **C**lostridium difficile
9. **E**ntamoeba histolytica

Causes of infectious watery diarrhea

1- Viruses

- Rota virus
- Norwalk and related viruses
- Adenovirus

2- Bacteria

- Vibrio cholera
- E .coli (enterotoxigenic)
- All bacteria causing bloody diarrhea

3- Protozoa

- Giardia lamblia
- Cryptosporidium

Causes of toxigenic diarrhea [food poisoning]

→ see infection

Causes of chronic diarrhea

1- **Infections**

- Giardia lamblia
- Entamoeba histolytica
- Tubercle bacillus
- Clostridium difficile
- Campylobacter and yersinia (rarely becomes chronic)

2- **Inflammations**

- Ulcerative colitis
- Microscopic colitis
- Collagenous colitis
- Crohn's disease (± concomitant bile salt and fat malabsorption)
- Ischemic colitis / enteritis
- Solitary rectal ulcer
- Diverticulitis / abscess

3- **Drugs**

- Laxatives
- Antibiotics
- Antacids
- Alcohol
- Diuretics
- Theophylline
- NSAIDs

4- **Malabsorption**

- Small bowel mucosal disease
  - Celiac disease
  - Tropical sprue
  - Whipple's disease
  - Lymphangiectasia
  - Lymphoma
  - Amyloidosis
  - Bowel resection / bypass
  - Carcinoid and radiation enteritis
- Disaccharidase deficiency (lactase)
- Pancreatic insufficiency (severe fat malabsorption)
  - Chronic pancreatitis
  - Cystic fibrosis

- Ischemic /radiation enteritis
- Short bowel syndrome
- Bacterial overgrowth of small intestine
    - DM
    - Diverticula of small bowel (large and multiple)
    - Scleroderma
    - Amyloidosis
    - Blind loop syndrome
- Postgastrectomy and enterostomy states

5- Endocrine

- Zollinger-Ellison syndrome (malabsorption)
- Hyperthyroidism
- Medullary thyroid cancer
- DM
- Carcinoid
- Non- β - cell pancreatic tumor
- Villous adenoma
- Tumors secreting vasoactive intestinal polypeptide
- Adrenal insufficiency

6- Motility disorders

- Irritable bowel syndrome
- Postvagotomy syndrome
- Postgastric surgery dumping syndrome
- Tumor/fecal impaction overflow diarrhea
- Narcotic bowel

7- **Incontinence of stool** (interpreted by the patient as diarrhea)

- Anal sphincter dysfunction
    - Anal fissures and fistulas
    - Perianal inflammation
    - Tears from childbirth
    - Anal intercourse or trauma
    - Diabetic neuropathy or neuromuscular diseases

Dysentery

Definition

1- Acute inflammation of the large intestine characterized by **diarrhea** with **blood** and **mucous** in the stool
2- Tenesmus also occur with rectal involvement

Causes

1- **A**moebic dysentery
2- **B**acillary desentery
3- **B**ilharzial desentery
4- **U**lcerative colitis
5- **C**ancer rectum
6- **D**iverticulosis

Acute gastrointestinal bleeding

Definitions

1- **Occult bleeding:**

- Initial presentation of a positive fecal occult blood test (FOBT) result and/or iron-deficiency anemia, when there is no evidence of visible blood loss to the patient or physician.

2- **Obscure bleeding:**

- Bleeding from the GI tract that persists or recurs without an obvious etiology after upper endoscopy, colonoscopy, and radiologic evaluation of the small bowel (such as by small bowel follow-through or enteroclysis).
- Subdivided into overt or occult, depending upon the presence or absence of clinically evident bleeding.

3- **Upper GIT bleeding**

- Refers to GI blood loss whose origin is proximal to the ligament of Treitz at the duodenojejunal junction i.e. (esophagus, duodenum and stomach).
- Acute UGIB can manifest in a variety of manners:
    - Haematemesis (vomiting of bright red blood or clots)
    - Coffee-ground emesis (by action of gastric acid on blood)
    - The return of bright red blood through a nasogastric tube
    - Melaena (black, tarry and offensive stools -not dark formed-): indicates moderate bleeding (blood has been in the GIT for 8 hr)
    - Haematochezia (red- or maroon-colored stool) may occur in patients with an extremely profuse UGIB (large volume of blood passes rapidly through the intestines).

4- **Lower GIT bleeding**

- Refers to GI blood loss whose origin is distal to the ligament of Treitz (last 1/4 of the duodenum and the entire area of the jejunum, ileum , colon, rectum and anus) → so, lower GIT bleeding include also small bowel bleeding

- Presented by :
  - Mainly, Bleeding per rectum (bright red blood) or Haematochezia
  - May be melena (right colonic lesions)

5- Small bowel bleeding

- From the ligament of treitze to the ileocecal valve
- Presented by :
  - Mainly, melena
  - Sometimes, bleeding per rectum or haematochezia
  - Unexplained anemia

6- Why bleeding is generally classified as either upper or lower in origin?

- Simply because the source of bleeding is only rarely in the jejunum or ileum
- Also because the presenting signs and symptoms frequently are characteristic of either an upper or a lower gastrointestinal source

Causes of upper GIT bleeding

1- Common

- Peptic ulcer disease (PUD)
  - Duodenal ulcer and duodenitis
  - Gastric ulcer
- Esophageal varices
- Acute erosive gastritis
  - NSAIDs
  - Stress ulcers
- Esophagitis
- Mallory – Weiss tear

2- Uncommon

- Gastric and duodenal varices
- Arteriovenous malformations
- Dieulafoy's lesions (ruptured mucosal artery)

- Upper GIT tumors and polyps
    - Esophageal cancer and lymphoma
    - Gastric cancer, lymphoma, leiomyoma and leiomyosarcoma
- Aortoenteric fistulae
- Esophageal rupture (Boerhaave's syndrome)
- Hemobilia (bleeding in the bile duct)
- Surgical anastomosis
- Coagulopathy
- Bleeding from nose or pharynx

Causes of lower GIT bleeding

1- **Common**

- Diverticular disease (40-55%)
    - Right sided lesions > left
    - 90% stop spontaneously
    - 10% rebleed in 1st year and 25% at 4 years
- Colonic angiodysplasia (3-20%)
    - Most common cause of SB bleeding in < 50 y/o
    - >50% are in right colon
- Colorectal cancer → Typically bleed slowly
- Colonic polyps
- Ischemic colitis
- Ulcerative colitis (15% of UC patients)
- Crohn's disease (1% of chron’s patients)
- Infectious colitis
- Internal haemorrhoids
    - >50% have hemorrhoids, but only 2% of bleeding attributed to them
- Anal fissure

2- **Uncommon**

- Meckel's diverticulum
- Radiation induced telangiectasia
- Dieulafoy's lesion

- Aorto-enteric fistula
- Vasculitis
- Hereditary haemorrhagic telangiectasia
- Blue rubber bleb nevus syndrome
- Anal cancer
- Rectal **u**lcer
- Rectal varices
- Post-polypectomy bleeding
- NSAID colopathy
- Antibiotic associated colitis
- Brisk upper GIT bleeding (rapid transport)
- Prostate biopsy site bleeding
- Endometriosis
- Amyloidosis and AIDS rarely

Causes of small bowel bleeding

1- **Angioectasias or arteriovenous malformations :**
  - 30 - 40% of causes (usually the age > 50yr)
  - These are abnormal blood vessels that lie within the wall of the small bowel
  - Associated with chronic kidney disease and valvular heart disease

2- **Ulcers of the small bowel**
  - Mainly due to NSAIDs

3- **Polyps**

4- Crohn's disease

5- Benign and malignant tumors

6- Blood vessels associated with certain heart conditions or cardiac implantable device

Approach to diagnosis of upper GIT bleeding

[This extended approach useful for oral and MCQ exam, in the final exam u should focuse only on the analysis and treatment of most common causes]

1- In general, **endoscopy** has become a keystone of both diagnosis and therapy

2- The importance of a **thorough history and physical exam** :

  - Allow rapid triage of patients who need medical ward or ICU-level care
  - Prioritise patients for urgent versus emergency endoscopy

History

1- Factors predictive of Upper GIT source of bleeding

  - Red blood or coffee grounds detected during nasogastric lavage
  - Reported history of melena
  - Melenic stool on examination
  - A ratio of blood urea nitrogen to serum creatinine > 30
  - On the other hand, the presence of blood clots in the stool made an upper GI source less likely

2- Coffee ground emesis

  - Is suggestive of a slower, possibly intermittent bleed (argues more for PUD and makes a variceal bleed less likely

3- Brisk haematemesis

  - Suggestive of an actively bleeding lesion, most often a variceal bleed (especially in patients with signs of liver disease or portal hypertension
  - Or an actively bleeding gastroduodenal ulcer.

4- Melena

  - Associated with UGIB rather than with lower GI bleeding (90%), though it may also originate from the terminal ileum or ascending colon (5%)
  - Indicates a more moderate rate of bleeding [seen with even 50 ml of blood]
  - Small bowel AVMs lead to chronic melaena

5- Haematochezia

  - Haematochezia is more often seen in LGIB than in UGIB.

- However, bright red blood per rectum can be seen in a brisk UGIB where the rapidity of the transit time precludes any digestion
  - Esophagogastric varices
  - Dieulafoy's lesions (may be intermittent)
  - Aortoenteric fistulae "herald bleed" (an episode of self-limiting bleeding before a massive bleed that can result in exsanguinations)
  - Eroded vessel in peptic ulcer
- Persistent or intermittent small amount of haematochezia renders an upper source less likely.

6- Symptom assessment

- Peptic ulcer: Epigastric or right upper quadrant pain, often improved transiently by ingestion of food
- Esophagaitis and esophageal ulcer: Odynophagia, gastroesophageal reflux, dysphagia
- Mallory-Weiss tear: nausea, vomiting, retching, or coughing prior to hematemesis (although many patients with a Mallory-Weiss tear have no history of vomiting). Also, seizures, hiccups, or straining can cause a tear
- Variceal hemorrhage or portal hypertensive gastropathy: Jaundice, weakness, fatigue, anorexia, abdominal distention
- Angiodysplasia or AVMs: usually painless, and patients can have chronic bleeding of which they are unware
- Malignancy: Dysphagia, early satiety, involuntary weight loss or night sweets
- The absence of nausea and vomiting: suggests a bleed distal to the pylorus
- Epistaxis or hemoptysis

7- Medication history

- PUD and erosive gastritis:
  - Often by Aspirin or other NSAIDs, alone
  - Or in combination with corticosteroids
  - And/or antiplatelet (e.g., clopidogrel) or anticoagulant agents (warfarin and plavix) simultaneously used esp. in patients with acute cardiovascular events.

- Pill esophagitis
    - Doxycycline, clindamycin, tetracycline and trimethoprim sulfa
    - NSAIDs
    - Ferrous sulfate
    - Theophylline
- Bismuth and iron supplements → can turn the stool black

8- Past medical history

- Prior episodes of upper GI bleeding → since up to 60 % of patients with a history of an upper GI bleed are bleeding from the same lesion
- Varices or portal hypertensive gastropathy → in a patient with a history of chronic liver disease,alcohol abuse or intravenous drug use
- Aorto-enteric fistula → in a patient with a history of an abdominal aortic aneurysm or an aortic graft
- Angiodysplasia or AVMs → in a patient with renal disease, aortic stenosis, hereditary hemorrhagic telangiectasia , advanced age or von Willebrand's disease
- Peptic ulcer disease in a patient with a history of Helicobacter pylori, smoking or past ulcers
- Malignancy in a patient with a history of smoking, alcohol abuse, or H. pylori infection
- Oesophagitis → in a patient with long-standing heartburn, globus sensation or hoarseness
- Mallory-Weiss tear → in a patient with hiatal hernia or alcohol use or advanced age
- Marginal ulcers (ulcers at an anastomotic site) → in a patient with a gastroenteric anastomosis
- Dieulafoy's lesions are regarded as congenital vascular aneurysms, yet they are most often symptomatic in men with alcohol histories, cardiovascular disease including hypertension, diabetes, or chronic kidney disease.
- Coagulopathy should be considered with history of genetic abnormalities of clotting (e.g., haemophilia, von Willebrand's disease), anticoagulant medications or liver disease

9- **Diet**

- Patients who have consumed large amounts of red gelatine or red-coloured beverages can interpret red-coloured vomitus as haematemesis.

Physical examination

1- **Assessment of severity of bleeding (Degree of anaemia/hypovolaemia) :**

- Mild to moderate hypovolemia: Resting tachycardia
- Blood volume loss of at least 15 % (>1 L): Orthostatic hypotension (a decrease in the systolic blood pressure > 20 mmHg and/or an increase in heart rate of 20 beats per minute when moving from recumbency to standing)
- Blood volume loss of at least 40 %: Supine hypotension
- Other factors associated with severe bleeding include
  - Red blood detected during nasogastric lavage
  - Bleeding per rectum esp during the first 4 hours of presentation
  - Hemoglobin level of < 8 g/dL
  - Significant drop in haematocrit from baseline (>6% to 8%)
  - Confusion and syncope
  - Cold/clammy extremities
  - Angina
  - Pallor
  - Systolic BP <115 mmHg
  - Heart rate >100 bpm
  - Non-tender abdomen
  - Aspirin use
  - More than 2 active comorbid states

2- **Visualizing the nares and the oropharynx**

- Identify a source of bleeding that does not require endoscopic management, as epistaxis or gingival bleeding

3- **A digital rectal examination is mandatory**

- Visual inspection of the perineum can rule out the presence of external haemorrhoids.
- Faecal occult blood testing should be conducted
  - Detected with as little as 15 mL of blood loss per day.

    - Stools may remain positive for occult blood for nearly 2 weeks after an acute blood loss of 1,000 mL or more from an upper gastrointestinal source

4- **Signs assessment**

- PUD → mid-epigastric tenderness to palpation is common.
- Variceal hemorrhage or portal hypertensive gastropathy: stigmata of chronic liver disease are often present:
    - Ascites, jaundice, Hepatomegaly or splenomegaly
    - Palmar erythema, Spider telangiectasias on the face, chest, or abdomen
    - Encephalopathy with or without asterixis
    - Caput medusa, Terry's nails or Gynaecomastia
- Esophagitis → reproducible pain can be demonstrated on swallowing
- Mallory-Weiss tear → Bleeding is sometimes accompanied by mid-epigastric pain or retrosternal pain
- Malignancy → cachexia, sometimes palpable abdominal mass and /or enlarged liver
- Aortoenteric fistulae → can present with significant abdominal or back pain and fever. Septic shock can occur, abdominal bruits or pulsatile masses can infrequently be detected
- Coagulopathy → may be stigmata of chronic liver disease
- Severe abdominal pain associated with rebound tenderness or involuntary guarding → raises concern for perforation.

Laboratory tests

1- CBC, serum chemistries, liver tests, and coagulation studies

- Coagulopathies with an INR >1.4 warrant correction with either vitamin K or fresh frozen plasma, or both
- Initial hemoglobin will often be at the patient's baseline because the patient is losing whole blood.
- With time (typically after 24 hours or more) the hemoglobin and hematocrit levels will decline (may take up to 72 hrs to equilibrate)
- Overhydration can lead to a falsely low hemoglobin value
- Hemoglobin level is monitored every 2 - 8 hours depending on severity

- Microcytic RBCs or iron deficiency anemia suggest chronic bleeding (acute bleeding should have normocytic RBCs)
- Leukocytosis: usually not in excess of 15,000/μL in UGIB but should not be attributed to acute blood loss without a search for sources of infection
- Platlets → normal or rarely thrombocytopenia in severe bleeding

2- **Blood group typing and cross-matching**

3- **Elevated BUN-to-creatinine** or urea-to-creatinine ratio (>20:1 or >100:1, respectively) can often be seen in UGIB (Because of absorbed blood proteins and decreased renal perfusion)

4- **Serial ECG and cardiac enzymes:** in patients who are at risk for a myocardial infarction, such as:
  - Elderly
  - History of coronary artery disease
  - Patients with symptoms such as chest pain or dyspnea

Nasogastric lavage [Controversial]

1- **Rationale**
  - Confirm NGT is in stomach.
  - Inject 250cc NS, then draw 250cc back or place to wall suction
  - Can be repeated for up to total of 2L
  - Stop when fluid is clear (or when reach 2L)

2- **Indications**
  - All patients with acute gastrointestinal bleeding unless the source is obviously the lower gastrointestinal tract

3- **Contraindications**
  - Facial trauma, nasal bone fracture
  - Known esophageal abnormalities (strictures, diverticuli)
  - Ingestion of caustic substances, esophageal burns
  - Generally, esophageal varices are NOT a contraindication to NG tube placement

4- **Interpretation of aspirate**
  - Bright red, clots = active UGIB

- Coffee grounds = slow bleeding, may have stopped, localizes to upper GI source
- Clear = indeterminate (NOT a guarantee that the bleeding has stopped)
- Nonbloody bilious = bleeding has stopped

5- Benefits

- To document the presence of blood (usually esophageal or gastric source and in more than 90% of bleeding duodenal ulcers)
- To monitor the rate of bleeding
- To identify recurrence of bleeding after initial control
- To lavage and decompress the stomach (remove particulate matter, fresh blood, or clots from the stomach to facilitate endoscopy)
- To remove gastric acid
- May contribute to hemostasis by allowing the walls of the stomach to collaps

6- Adverse effects

- Patient discomfort
- Predisposition to gastroesophageal reflux and pulmonary aspiration
- Irritation of the esophageal and gastric mucosae, creating mucosal artifacts and aggravating existing lesions

Upper GIT endoscopy (OGD)

1- Benefits

- The corner stone of diagnosis and treatment for most causes of UGIB
- Early endoscopy (within 24 hours of hospital admission) has a greater impact than later endoscopy on length of hospital stay and requirements for blood transfusion.
- Up to 46% of haemodynamically stable patients who are evaluated for UGIB with upper endoscopy, and subsequently are found to have low-risk stigmata for recurrent bleeding, can be safely discharged and followed as outpatients.

2- Diagnostic findings

- PUD

  - Direct visualisation of sharp punched out deep ulcer
  - Stigmata of recent hemorrhage (SRH) within an ulcer crater include a protruding visible vessel, an adherent clot, a black eschar, and actual oozing or spurting of blood. Patients with SRH are more likely to have uncontrolled or recurrent bleeding
  - A biopsy of the gastric mucosa should be taken for H.pylori infection and exclusion of gastric carcinoma

- Esophageal varices
  - Direct visualization of bleeding or varices
  - Endoscopic stigmata in patients with varices and no other visible source of bleeding (Endoscopic red color signs): red weals, cherry-red spots, hematocystic spots
- Mallory wises tear
  - Direct visualisation of intramural dissections
- Esophagitis
  - Superficial ulcers or erosions and diffusely friable hemorrhagic mucosa with exudates
  - Deep punched out esophageal ulcers and strictures
- Gastric varices → classically seen in cardia of stomach (usually extends > 5cm below the gastroesophageal junction)
- Portal hypertensive gastropathy → friability of the mucosa and the presence of dilated blood vessels at the surface
- AVMs → direct visualisation of centrifugally expanding dilated capillaries
- Dieulafoy's lesions → Submucosal vessels that dive towards the gastric lumen
- Upper GIT tumors → direct visualisation of mass or malignant ulcer and positive histology
- Aortoenteric fistula → direct visualisation of fistula
  - Graft protruding through the bowel wall
  - Or fresh bleeding in distal duodenum

- Or adherent clot or extrinsic compression by a pulsating mass with a suture line protruding into the duodenum

CT angiograpgy

1- Esophagogastric varices → show collateral veins and recanalised umbilical vein

2- AVMs → accumulation of vessels in the bowel wall, early filling vein or enlarged supplying artery

Endoscopic U/S

1- Upper GIT tumors → useful in making initial diagnosis and subsequent local staging

2- Dieulafoy's lesions → identification of lesion in very rare cases not seen by endoscopy

Abdominal CT

1- Upper GIT tumors → useful in making initial diagnosis and detection of distant metastases (PET-CT)

2- Aortoenteric fistula → contiguity of aorta with bowel (aortography and U/S can be useful)

Approach to diagnosis of lower GIT bleeding

[This extended approach useful for oral and MCQ exam, in the final exam u should focuse only on the analysis and treatment of most common causes]

History

1- Age of patient:

- Typically > 60-65yr → Diverticular disease , angiodysplasia, and ischemic colitis
- Typically > 40yr → colonic polyps and colorectal cancer
- Inflammatory bowel disease or a Meckel's diverticulum is more likely in a child or young adults

2- Duration of the bleeding

- Intermittent or chronic rectal bleeding → usually seen in patients with internal haemorrhoids.
- Acute bleeding, especially in older people → should prompt evaluation for diverticular disease

3- Colour of the blood

- Helps to localise the site of bleeding
- As well as whether the blood coats the stools or is mixed with the stools

4- Symptoms assessment

- Diverticular disease → mild or severe painless haematochezia, stops spontaneously in most, recurrent bleeding in 10% - 40% of patients
- Colonic angiodysplasia → intermittent, mild, or severe episodes of painless haematochezia
- Ischemic colitis → sudden-onset lower abdominal cramping, diarrhoea, and self-limited haematochezia
- Ulcerative colitis → haematochezia; chronic diarrhoea; lower abdominal pain; faecal urgency; tenesmus; episodes of constipation; weight loss; acute arthropathy; symptoms can be intermittent
- Infectious colitis → acute diarrhoea, abdominal pain
- The presence of abdominal pain and diarrhoea with haematochezia → suggests colitis, either inflammatory or ischaemic,
- Colorectal cancer or inflammatory colitis → Change of bowel habit, tenesmus, weight loss or abdominal pain
- Colonic polyps → asymptomatic, change in bowel movements, abdominal pain
- Internal haemorrhoids → self-limited, intermittent, painless bright red rectal bleeding; constipation may also be present; blood may be covering the stool
- Anal fissure → rectal bleeding (usually seen on wiping) and severe peri-anal pain on defecation
- Meckel's diverticulum → painless melaena or bright red blood per rectum (described as 'currant jelly') is the major symptom
- Radiation enteritis or colitis (radiation induced telangectasia) → diarrhoea, rectal pain or urgency, faecal incontinence, and obstructed defecation may also

occur; symptoms typically 9 weeks to 4 months after radiation injury; bleeding may be persistent or severe

- Aorto-enteric fistula → , melaena, and haematemesis and herald bleed may occur
- Vasculitis → abdominal pain, nausea, vomiting, haematemesis and bleeding per rectum
- Hereditary haemorrhagic telangiectasia → epistaxis
- Rectal ulcer → rectal bleeding; passage of mucous; straining during defecation; and sense of incomplete evacuation

5- Medical history

- Aspirin/NSAID use → NSAID colopathy
- Recent antibiotic use → antibiotic associated colitis
- Constipation-inducing drugs → Ischemic colitis
- Bismuth and iron supplements → can turn the stool black

6- Past medical history

- Diverticular disease → may be a hx of recurrent left lower abdominal pain, bloating, constipation and diarrhea
- Colonic angiodysplasia → may be hx of end-stage renal disease, von Willebrand's disease, aortic stenosis, or anticoagulant therapy
- Ischemic colitis → may be hx of haemodialysis, hypertension, hypo-albuminaemia, diabetes mellitus, constipation-inducing drugs
- Crohn's disease → chronic diarrhoea (usually non-bloody); symptoms can be intermittent; tenesmus; gradual onset of symptoms; weight lossu
- Ulcerative colitis → hx of primary sclerosing cholangitis
- Infectious colitis → may be a history of recent travel to regions with higher risk of infectious diarrhea
- Colonic polyps → may be FHx of colonic polyps, colon cancer, or familial adenomatous polyposis or Gardner's syndrome
- History of anal lesions
- Radiation enteritis or colitis (radiation induced telangectasia) → Previous abdominal or pelvic irradiation (acute effects of irradiation on the gut, or bleeding may occur months to years later).

- Aorto-enteric fistula → in a patient with a history of an abdominal aortic aneurysm or an aortic graft
- Vasculitis → history of vasculitis (such as SLE, polyarteritis nodosa)
- Hereditary haemorrhagic telangiectasia → FHx of hereditary haemorrhagic telangiectasia
- Post-polypectomy bleeding → history of colonoscopy within the last 3 weeks
- Prostate biopsy site bleeding → rectal bleeding at a few hours or days after a prostate biopsy
- Endometriosis → female gender, reproductive age, may be a hx of dysmenorrhoea, pelvic pain, dyspareunia, infertility

Physical examination

1- Assessment of severity of bleeding (Degree of anaemia/hypovolaemia) :

- Mild to moderate hypovolemia: Resting tachycardia
- Blood volume loss of at least 15 % (>1 L): Orthostatic hypotension (a decrease in the systolic blood pressure > 20 mmHg and/or an increase in heart rate of 20 beats per minute when moving from recumbency to standing)
- Blood volume loss of at least 40 %: Supine hypotension
- Other factors associated with severe bleeding include
    - Red blood detected during nasogastric lavage
    - Hemoglobin level of < 8 g/dL
    - Significant drop in haematocrit from baseline (>6% to 8%)
    - Confusion and syncope
    - Cold/clammy extremities
    - Angina
    - Pallor
    - Systolic BP <115 mmHg
    - Heart rate >100 bpm
    - Non-tender abdomen
    - Bleeding per rectum during the first 4 hours of presentation
    - Aspirin use
    - More than 2 active comorbid states

2- Signs assessment

- Diverticular disease and Colonic angiodysplasia → vital signs may indicate severe bleeding and (may be indistinguishable but in diverticular disease bleeding is usually more profuse and more likely to cause haemodynamic instability)
- Ischemic colitis → lower abdominal tenderness. Presence of peritoneal signs/absence of bowel sounds may suggest trans-mural infarction or perforation
- Crohn's disease → patient may appear pale, malnourished, right lower quadrant abdominal tenderness, may be abdominal mass or mild fever, oral ulceration, peri-anal skin tags, fistulae, abscess or sinus tract. Life threatening bleeding rare
- Ulcerative colitis → patient may appear pale, malnourished, abdominal tenderness, erythema nodosum or pyoderma gangrenosum, uveitis or episcleritis, fever may be present. Life threatening bleeding rare
- Infectious colitis → mild fever and abdominal tenderness may be present
- Colorectal cancer → palpable abdominal mass or hepatomegally may be present
- Meckel's diverticulum → abdominal tenderness and abdominal mass may be present
- Dieulafoy's lesion → vital signs may indicate severe bleeding
- Aorto-enteric fistula → vital signs may indicate severe bleeding, fever may be present
- Upper GIT bleeding → may be epigastric tenderness and vital signs may indicate severe bleeding
- Vasculitis → stigmata of underlying vasculitic condition (e.g. malar butterfly rash in SLE) and abdominal tenderness may be present
- Hereditary haemorrhagic telangiectasia → multiple telangiectasia on lips, oral cavity, fingers and nose
- Blue rubber bleb nevus syndrome → multiple cutaneous lesions (protuberant dark blue vascular tumors) may be seen. Skeletal bowing may be present if there is bone involvement
- Rectal varices → stigmata of chronic liver disease

- Endometriosis → lower abdomen tenderness; pelvic examination may reveal pelvic mass (ovarian endometrioma), fixed and retroverted uterus or uterosacral ligament nodularity and tenderness

3- **Rectal examination**

- Essential to exclude a palpable rectal mass
- Anal fissure may be visible, most commonly in the posterior midline (consider anaesthesia if PR would be too painful)

Investigations

Initial tests

1- **CBC, serum chemistries, liver tests, and coagulation studies**

- Coagulopathies with an INR >1.4 warrant correction with either vitamin K or fresh frozen plasma, or both
- Initial hemoglobin will often be at the patient's baseline because the patient is losing whole blood.
- With time (typically after 24 hours or more) the hemoglobin and hematocrit levels will decline (may take up to 72 hrs to equilibrate)
- Overhydration can lead to a falsely low hemoglobin value
- Hemoglobin level is monitored every 2 - 8 hours depending on severity
- Microcytic RBCs or iron deficiency anemia suggest chronic bleeding (acute bleeding should have normocytic RBCs)
- Leukocytosis: in inflammatory,ischemic or infectious conditions
- Platlets → normal or rarely thrombocytopenia in severe bleeding

2- **Blood group typing and cross-matching**

3- **Elevated BUN-to-creatinine** or urea-to-creatinine ratio (>20:1 or >100:1, respectively) can often be seen in UGIB (Because of absorbed blood proteins and decreased renal perfusion)

4- **ESR and CRP:** may be elevated in patients with inflammatory bowel disease.

5- **Stool studies** in patients with haematochezia associated with acute diarrhoea.

- Stool WBC → ↑ in infectious colitis
- Stool culture
- Microscopic examination for ova and parasites

6- **Serological markers**

  - ANA, ANCA → if the bleeding is suspected to be 2ry to a vasculitic disease such as systemic lupus erythematosus

7- **Serial ECG and cardiac enzymes:** in patients who are at risk for a myocardial infarction, such as:

  - Elderly
  - History of coronary artery disease
  - Patients with symptoms such as chest pain or dyspnea

Nasogastric tube lavage (in all patients with severe bleeding)

1- To rule out the upper GI tract as the source of the bleeding.

2- A bleeding source in the upper GI is present in 11% of patients with haematochezia

Anoscopy

1- In patients with a suspected anorectal source of bleeding

2- Internal haemorrhoids and anal cancer can be visualised

Colonoscopy

1- **Indications :**

  - Colonoscopy is the initial imaging procedure in all patients with suspected lower GI bleeding in whom an upper GI or anorectal source have been excluded (both diagnostic and therapeutic).

2- **Urgent colonoscopy**

  - Requires a bowel preparation (often with polyethylene glycol solution).with diagnostic yield between 48% and 90%.

3- **Complications**

  - Adverse reactions to the IV sedative drugs
  - A low risk of perforation.

4- **Diagnostic findings**

  - Diverticular disease
    - Active bleeding or fresh blood may be seen along with diverticulae
  - Colonic angiodysplasia

  - 5 - 10 mm cherry red, ectatic blood vessels radiating from a central vessel
  - Angiomas often multiple and may occur in both large and small intestine
- Ischemic colitis → petechial haemorrhages, oedema, ulceration of colonic mucosa (usually performed after CT to confirm the diagnosis)
- Crohn's disease
  - Friable, ulcerated, oedematous mucosa
  - Skip lesions (normal appearing bowel in between abnormal sections).
  - Biopsies are diagnostic
- Ulcerative colitis
  - Rectal involvement
  - No skip areas
  - Loss of vascular marking, diffuse erythema, mucosal granularity, fistulas (rarely seen), normal terminal ileum (or mild 'backwash' ileitis in pancolitis).
  - Biopsies are diagnostic.
- Colorectal cancer and polyps→ friable mass or polyps in the colon may be seen and biopsy is diagnostic
- Radiation-induced telangiectasia → mucosal pallor with friability and telangiectasias (mucosal biopsy not needed to confirm the diagnosis)
- Dieulafoy's lesion → a superficial blood vessel may be seen in the colon at the site of bleeding
- Hereditary haemorrhagic telangiectasia → telangictasia present in the lower GIT
- Blue rubber bleb nevus syndrome → protuberant dark blue vascular lesions are seen in the GI tract
- Rectal varices → vascular structures extending proximally from the dentate line
- Endometriosis → endometriotic lesions visualized

- NSAID colopathy → erosions and ulcerations in the colon may be seen
- Rectal ulcer → erythema, ulcerations, polypoid lesions (histological findings are characteristic)
- Post-polypectomy bleeding and Prostate biopsy site bleeding → bleeding at the site of the procedure

Radionuclide imaging [tagged RBC scintigraphy, for example, technetium scanning]

1- **Indications**
   - In persistent bleeding with a normal colonoscopy and OGD

2- **Advantages**
   - Localise the source of even minimal bleeding (as little as 0.1 mL/minute).
   - It can be used as a screening procedure prior to mesenteric angiography, since patients with a negative scan are unlikely to benefit from angiography.
   - Non-invasive and safe.

3- **Disadvantages** → Ineffective if bleeding has ceased with no therapeutic role

4- **Diagnostic findings:**
   - Diverticular disease → scintigraphy demonstrates extravasation and identifies the site of bleeding
   - Colonic angiodysplasia → may localise bleeding site
   - Meckel's diverticulum → shows an uptake due to technetium binding to the ectopic gastric parietal cells(the sensitivity of the test is improved by use of pentagastrin or cimetidine)

Mesenteric angiography

1- **Indications:**
   - Persistent GI bleeding with negative colonoscopy

2- Radionuclide imaging study is often needed **prior to angiography**

3- **Advantages:**
   - Accurate localisation of a rapidly bleeding site
   - Offers possible therapeutic options

4- **Disadvantages**

- Possible risk of complications such as renal failure, arterial thrombosis, and contrast reactions.
- Requires an active blood loss for a bleeding site to be visualised.

5- **Diagnostic findings**

- Diverticular disease → localises the site of bleeding, if the bleeding rate is >0.5 mL/minute
- Colonic angiodysplasia → may localise active bleeding site
- Meckel's diverticulum → extravasation of the dye at the bleeding site in the terminal ileum

CT abdomen

1- **Indications and diagnostic findings:**

- Ischaemic colitis [1st test] → segmental circumferential wall thickening
- Aorto-enteric fistula:
    - Peri-graft fluid, soft tissue attenuation, ectopic gas, pseudo-aneurysm, or focal ischemic bowel
    - Sensitivity and specificity are 95 and 85% respectively if these typical findings present
    - Exploratory laparotomy is the definitive method for diagnosis
- Vasculitis → may show thickening of the wall of the colon or the small intestine (colonoscopy and OGD should be avoided if possible)

2- **CT angiography** can be performed in place of catheter-based mesenteric angiography

3- **CT angiography has a sensitivity** of 89% and specificity of 85% in patients with acute gastrointestinal bleeding.

OGD

1- **Indications and diagnostic findings:**

- The recommended diagnostic test in patients suspected to have upper GI bleeding → erosions, ulcerations or actively bleeding vessels may be seen
- Aorto-enteric fistula → bleeding from the 2nd or 3rd part of duodenum may be visualized (sensitivity 25% and CT scan of the abdomen is needed to confirm the diagnosis)

    - Hereditary haemorrhagic telangiectasia → telangiectasia present in the upper GI tract (more common in stomach and duodenum than colon)
    - Blue rubber bleb nevus syndrome → protuberant dark blue vascular lesions are seen in the GI tract

2- Transvaginal U/S

    - Ovarian endometrioma: homogeneous, low level echoes
    - Deep pelvic endometriosis such as uterosacral ligament involvement: hyperechoic linear thickening

General management of acute GIT bleeding

Goals of care

1- Stabilize patient's **hemodynamics**

2- Assess patient, determine source of bleed

3- Stop any active bleeding

4- Treat underlying **cause**

5- Prevent **recurrence**

Principles of initial management

1- Perform in order determined by activity of bleeding

- History, including previous bleeding and endoscopies
- Vital signs, including postural signs
- Physical examination including rectal examination
- Insertion of large bore peripheral venous catheter and if necessary, a central venous line
- Withdrawal of blood for initial laboratory studies
- Administration of I.V. electrolyte solutions and blood

2- Pass a NGT ®

- If clear initially or clear promptly with lavage, remove

- If bloody, leave in to monitor bleeding and to provide acess to GIT

3- **Survey for concomitant** heart, lung, renal, liver or CNS disease

4- **Consult** a gastroenterologist, a surgeon and if indicated, a radiologist

5- Make a **diagnosis** (investigations) and start **specific treatment**

Resuscitation

1- **A**ir way

2- **B**reathing

3- **Circulation**

- Establish blood access [2 large bores, ideally at least 18-gauge peripheral IVs]
- Is the patient orthostatic? [require loss of 20% of blood volume and the patient becomes dizzy when I get up)
- Is the patient in shock? [require loss of 40% of blood volume and the patien is hypotensive, tachycardic with pallor and cold sweets]
- Replace intravascular volume
  - If orthostatic and/or hypotensive → give normal saline boluses
  - If anemic (Hb <8 g/dl) → give packed RBCs
  - If INR > 1.4 or massive bleeding → may need fresh frozen plasma , vitamin K or platelets infusion (Extensive fluids dilutes platelets and clotting factors, particularly factors V and VII)
  - Electrolytes and clotting factors given if needed
- Monitor urine output
- If hypernatremia present e.g. ascites and peripheral edema :
  - If the patient is bleeding profusely and blood for transfusion is not yet available, saline should be infused without regard for the patient's sodium balance
  - If bleeding is less severe, hypotonic solutions may be infused until blood transfusion arrives
- Frequent assessment of serum electrolytes, calcium, phosphate, and magnesium levels is necessary

- Patients who receive > 100 mL of blood per minute may be given 0.2 g calcium chloride ($CaCl_2$) via another intravenous line during the time the blood is infusing (hypocalcemia as a result of binding of calcium by anticoagulants in banked blood may occur after massive transfusions)

Indications for ICU admission

1- Hemodynamic instability despite adequate volume resuscitation

2- NG lavage does not clear with 2 L

3- History of cirrhosis (concern for variceal bleed)

4- Continued bleeding

Be concern with

1- Age > 60
2- Multiple comorbidities
3- Coagulopathy (warfarin, plavix, cirrhosis)
4- Known portal HTN
5- Hematemesis is bright red blood
6- History of AAA repair

Risk stratification in UGI bleeding

1- **Very low risk endoscopic findings:**

- Clean-bsed ulcer
- Clean based Mallory-Weiss tear
- Gastritis/duodenitis/esophagitis
- Portal hypertensive gastropathy

Discharge if stable

2- **Medium risk endoscopic findings**

- AVM's
- Ulcer with stigmata of recent hemorrhage
- Mallory-Weiss with stigmata of recent hemorrhage
- Varices with active bleeding
- Cancer

Hemostasis and medical ward

3- **High risk endoscopic findings**

- Active ulcer bleeding

- Active variceal bleeding
- Active bleeding Dieulafoy’s lesion

Hemostasis and ICU admission

Rockall's risk score

1- Score that **predicts poor prognosis**, i.e. death, from upper GI haemorrhage

2- It uses clinical criteria (increasing age, co-morbidity, shock) as well as endoscopic finding (diagnosis, stigmata of acute bleeding)

Variable	**Score**			
	0	1	2	3
Age (years)	<60	60-79	>80	
Shock **Pulse rate** **SBP (mmHg)**	“No shock” < 100 > 100	“Tachycardia”, > 100 > 100	“Hypotension” < 100	
Comorbidity	No		Cardiac failure, ischaemic heart disease, any major comorbidity	Renal failure, liver failure, disseminated malignancy
Diagnosis	Mallory-Weiss tear, no lesion identified and no SRH/blood	All other diagnosis	Malignant lesion of UGIT	
Major SRH	None or dark spot only		Blood in the UGIT, adherent clot, visible or spurting vessel	

Score	**% of Total**	**Rebleeding**	**Death**
0	5.6	4.9	0
1	11	3.2	0
2	12.8	5	0.3

3	15.9	12.2	2
4	17.8	13.8	4.2
5	14.5	16.9	7.9
6	9.4	29.4	15.1
7	8	39.6	19.8
>8	5.1	47.7	39.1

Specific management for upper GIT bleeding

Medical therapy

1- PUD

- I.V. PPIs bolus of 80 mg then drip at 80 mg/hr for 72 hr
    - Has shown to accelerate resolution of bleeding and decrease need for therapy during OGD
    - The reduction of intraluminal acid may be effective in two ways. First, the direct, harmful effects of acid and pepsin on the bleeding lesion are diminished. Second, a less acid environment allows platelets to aggregate and thus promotes clotting

2- Varices

- Octreotide 50-100 mcg bolus then 50 mcg/hr drip
- If the patient had ascites, will need antibiotics for 7 days for prophylaxis against SBP
    - Norfloxacin 400 mg / 12 hr orally
    - Ciprofloxacin 500 mg /12 hr orally

Endoscopic therapy

1- Bleeding duodenal ulcer

- The bleeding artery is the gastroduodenal artery
- Mathods of stopping bleeding:

    - Adrenaline 1:10000
    - Cautery
    - Argon plasma coagulation
    - Hemoclip
    - Hemostatic spry
- Combining injection therapy with electrocoagulation may have added benefits and is currently being widely used
- The bleeding stops and the patient stays 1-2 days NPO, given PPIs for **6 weeks** plus eradication of **H.pylori**
- The patient can eat or drink after 1-2 days

2- Bleeding gastric ulcer

- The same modalities as duodenal ulcer but PPIs given for **8 weeks** plus eradication of **H. pylori**
- Peptic ulcer could be malignant, so **biopsy** recommended

3- Esophageal or gastric varices

- High mortality and morbidity with high recurrence rate
- Initial treatment:
    - Rubber band ligation for esophageal varices
    - Histoacryl injection for fundal varix
- Injection sclerotherapy (ethanolamine)
- Blackemore –Sengstaken tube
- TIPS
- Gastric transaction

4- Mallory weiss tear

- 90% in the cardia and 10% in the esophagus
- Often stops spontaneously in most patients
- Local injection of adrenaline at endoscopy, endoscopic placement of clips or bipolar electrocautery
- If persistent bleeding → direct suturing at laparotomy
- May be expected to heal in several days without specific therapy.

5- Dieulafoy's disease

- Found in the fundus of stomach –J maneuver
- Endoscopic hemostasis
    - Adrenaline injection, hemoclips, injection sclerotherapy, heater probe or laser photocoagulation

6- **Portal hypertensive gastropathy**
   - Argon plasma coagulation
   - TIPS

7- **Aorto enteric fistula**
   - High morbidity and mortality despite treatment (75%)
   - Bleeding may stop abruptly
   - If bleeding recurs → emergency extensive reconstructive surgery is required

8- **Erosive gastritis and stress ulcers**
   - Gastric wash by cold saline and antacids by ryle tube
   - I.V. PPIs or ranitidine
   - Misoprostol (100-200 µg 4 time/day) can be used
   - Typically heals rapidly after withdrawal of the offending agent (aspirin, alcohol) and correction of the general condition and use of acid suppressive drugs

Important causes of abdominal masses

Right iliac fossa mass

1- **A**ppendix mass
2- **C**ancer colon
3- **C**rohn's disease (adherent bowel loops)
4- **I**leocecal TB

5- **P**soas abscess

6- **T**ransplanted kidney (note any overlying scar)

Left iliac fossa mass

1- **D**iverticular abscess

2- **P**soas abscess

3- **C**ancer colon

4- **T**ransplanted kidney

Midline mass

1- **A**ortic aneurysm

2- **C**ancer stomach

3- **O**varian cysts

4- **B**ladder (retension of urine)

5- **P**ancreatic pseudocyst

6- **C**ancer pancreas

7- **H**orseshoe kidney

8- **U**terine masses

Focal splenic lesions

Hypoechoic lesions	**Hyperechoic lesions**
1- Cystic lesions	1- Cysts with hemorrhage

2- Metastases 3- Abscesses 4- Acute hematoma 5- Hemangioma 6- Acute infarction 7- Lymphoma* 8- Lymphangioma*	2- Metastasis 3- Abscesses 4- Subacute hematoma 5- Hemangioma 6- Subacute or chronic infarction 7- Calcification*

Cystic lesions

1- 1ry
    - Parasitic e.g. E.granulosus and T. solium
    - Non-parasitic : either congenital as dermoid and epidermoid cysts or neoplastic

2- 2ry after
    - Trauma
    - Infarction
    - Infection (malaria, EBV, TB)

Abdominal pain

Causes of Upper abdominal pain

Esophagus	GERD, Hiatus hernia , esophagitis, carcinoma
Gastrodudenal	Peptic ulcer, gastritis, gastric carcinoma, pyloric stenosis
Gall bladder	Acute and chronic cholecystitis, gall stones
Pancreas	Acute and chronic pancreatitis, cancer pancreas
Hepatic	Viral hepatitis, amoebic hepatitis, congested liver, carcinoma
CVS	Angina, myocardial infarction, pericarditis, dissecting aneurysm
Chest	Diaphragmatic pleurisy
Intestine	Irritable bowel syndrome, bowel obstruction
Miscellaneous	Lower rib pain, Herpes zoster, fatty hernia of linea alba, myositis, diabetic ketoacidosis, nephrolithiasis (pain may radiate to right upper quadrant)

Causes of acute abdominal pain

Inflammation	- Cholecystitis - Pancreatitis - Penetrating ulcer into pancreas - Appendicitis - Diverticulitis - Hepatitis - PID - Peptic ulcer - Gastroenteritis - SBP - 2ry bacterial peritonitis - Acute colitis - Pyelonephritis or cystitis - Acute cholangitis - Mesenteric lymphadenitis - Abdominal abscess - Regional enteritis - Toxic megacolon (usually due to UC)
Mechanical	- Small or large bowel obstruction - Volvulus - Biliary obstruction - Ureteral stones - Intussusception - Intraabdominal adhesions
Ruptured or perforated viscus	- Spontaneous pneumothorax - Ruptured or dissecting aortic aneurysm - Ruptured ectopic pregnancy - perforated peptic ulcer - Ruptured spleen - Ruptured esophagus (Boerhaave's syndrome) - Ruptured stomach (usually due to trauma) - Ruptured diverticulum (Meckel's, colonic) - Ruptured cyst or tumor
Ischemic	-Mesenteric ischemia - Splenic infarction - Testicular tortion - Ovarian cyst tortion - Incarcerated hernia - MI - Pulmonary embolism
Metabolic	- Diabetic ketoacidosis - Uremia - Porphyria

	- Lead poisoning
Others	-Thoracic disorders - Herpes zoster - SLE - Musculoskeletal disorders - Functional abdominal pain - Irritable bowel syndrome - FMF - Narcotic withdrawal - Hereditary angioedema - Sickle cell disease - Henoch Schonlein purpura - Vaculitis - Pleurisy - Cord compression (thoracic segments)

Non cardiac chest pain

Chest wall pain	- Costochondritis - Trauma
Mediastinal pain	-Inflammation - Tumor
Esophageal pain	- Motility disorders * Achalasia (usually vigorous achalasia) * Diffuse esophageal spasm * Nutcracker esophagus * Nonspecific motor disorder
	- Mucosal disorders * GER ± gross injury * Viral or fungal esophagitis * Acid or alkali ingestion * Cancer
Gall bladder disease	- Acute or chronic cholecystitis - Stones
Pancreas	- Pancreatitis - Pancreatic pseudocyst
Stomach , intestine	- Peptic ulcer
Cardiac chest pain (initial Failure to diagnose)	- Coronary artery disease - Pericarditis

Differential diagnosis of nausea and vomiting

Gastrointestinal disorders	- Peptic ulcer disease - Nonulcer dyspepsia - GERD - Acute gastritis - Gastroparesis - Gastric outlet obstruction - Cancer stomach - Functional disorders: functional nausea and vomiting, chronic idiopathic nausea - Inflammation of any viscus: Appendicitis, hepatitis, pancreatitis, diverticulitis, colitis, cholecystitis - Biliary colic and Gall stones - Small bowel obstruction or late large bowel obstruction - Mesenteric ischemia - Intestinal pseuo-obstruction
Infections	- Gastroenteritis: viral (Rotavirus, Norwalk virus, Adenovirus, Reovirus), bacterial (S. aureus, Salmonella, Bacillus cereus, Clostridium perfringens) - Systemic nongastrointestinal infections - Otitis media, acute hepatitis,…. - UTI (pyelonephritis), renal colic
CNS disorders	-Increased intracranial pressure: tumor, hemorrhage, pseudotumor cerebri, meningitis, encephalitis

	- Migraine - Psychogenic vomiting - Cyclic vomiting syndrome - Anorexia nervosa - Bulimia nervosa - Vestibular disorders: Labyrinthitis, motion sickness, Meniere's disease, cerebellopontine angle tumors
Medications	- Chemotherapy: cisplatin, dacarbazine, nitrogen mustard [serotonergic pathways] - Analgesics and NSAIDs [vomiting center] - Opioid analgesics - Oral contraceptives - Cardiovascular: digoxin, antiarrhythmics, beta blockers, antihypertensives, calcium channel blockers - Antibiotics: erythromycin, tetracycline, sulfonamides [vomiting center] - Sulfasalazine - Azathioprine - Antiparkinsonian agents e.g. bromocriptine, L.dopa [CTZ] - Theophylline - Cannabis (Cannabinoid hyperemesis)
Endocrine and metabolic	- Pregnancy, hyperemesis gravidarium - Uremia - Diabetic ketoacidosis - Addison's disease - Hyperparathyroidism - Hypercalcemia -
Other disorders	- Postoperative nausea and vomiting - Cardiac ischemia or infarction, congestive heart failure - Glucoma - Salpingitis - Torsion of ovarian cyst

Intestinal gas and bloating

Belching	- GERD - Peptic ulcer disease - Gastric carcinoma

	- Gastroparesis - Gastric outlet obstruction - Uremia - Gall bladder disease - Nervous habit - Chronic gastric stasis or gastrocolic fistula - Ingestion of excessive carbonated beverages
Abdominal pain and bloating	- Irritable bowel syndrome - Lactase deficiency - Celiac sprue - Regional enteritis - Recurrent partial small bowel obstruction - Giardiasis
Excessive flatulence	- Disorders of intestinal motility - Lactase deficiency

Index & questions

Infectious esophagitis

GERD

- Discuss DD, lifestyle, medical & surgical treatment of GERD
- Discuss therapeutic options of GERD
- Discuss complications of GERD

Eosinophilic esophagitis

Esophageal strictures

Barrett's esophagus

- Barrette’s disease of esophagus can be a serious disease, explain its management
- Give an account on Barrett's esophagus

Esophageal cancer

Esophageal motility disorders

Globus

Hiatus hernia

H.pylori infection

- Describe the management of H .pylori and its complications
- Discuss diagnosis and treatment of H.pylori infection

Acute gastritis

Chronic gastritis

- Give short account on variant gastric disease causing anemia

Gastric carcinoma

- Discuss clinical picture, investigations and treatment of gastric lymphoma

Intestinal TB

- Discuss intestinal TB

Malabsorption syndrome

Celiac disease

- Discuss adult celiac disease as regard management
- Discuss diagnosis and treatment of glutin sensitive enteropathy

Tropical sprue

Whipple's disease

- Explain the cause, clinical picture, diagnosis and treatment of whipple’s disease

Small bowel bacterial overgrowth

Ileal resection

Short bowel syndrome

Radiation enteritis and proctocolitis

Abetalipoproteinemia

Food allergy and lactose intolerance

Dermatitis herpitiform

Colonic polyps

- Types & management of colonic polyps
- Colonic polyposis: full account
- Colonic polyps: different types and its clinical significance
- Mention causes and management of intestinal polyps

Ulcerative colitis

- Describe the treatment of a case of ulcerative colitis with emphasis on new drugs used

- Extra-intestinal manifestations of inflammatory bowel diseases
- Inflammatory bowel disease developed right upper abdominal pain with jaundice: how to proceed in this patient to diagnosis
- Discuss treatment of ulcerative pancolitis of mild to moderate activity
- Discuss treatment of ulcerative colitis

Crohn's disease

- Give an account on crohn’s disease
- Give differences in management between crohn's disease and ulcerative colitis as regard diagnosis and treatment

Colorectal cancer

Irritable bowel syndrome

Chronic pancreatitis

- Tropical calcific pancreatitis: account
- Discuss causes, complications and treatment of chronic pancreatitis

Acute pancreatitis

- A patient presents with possible diagnosis of acute pancreatitis, describe clinical picture, investigations and treatment of this case
- Give an account on acute pancreatitis

Pancreatic pseudocysts

Pancreatic cancer

Dysphagia

- Give an account on esophageal causes of dysphagia and their management

Constipation

- 50 years old female complain of obstinate constipation for the last 2 months, explain how to manage
- Define constipation: how to diagnose a case of constipation in 60-70 years old man

Diarrhea

- Discuss causes & management of a case of acute infectious diarrhea
- Give an account on acute infectious diarrhea
- Discuss chronic dysenteries
- How to reach diagnosis in a case presented with tenesmus
- Secretory diarrhea
- How to manage bloody diarrhea
- Give account on traveler's diarrhea
- Non-infectious causes of diarrhea: enumerate causes, design approach and discuss treatment of 2 causes

Acute GIT bleeding

- Explain in details the management of a case presenting with upper GIT bleeding
- Clinical approach for occult GI bleeding
- Management of suspected small bowel bleeding

- Management of hematemisis

GIT manifestations of infectious diseases

- The patient with HIV may have many GIT problems, describe the clinical picture of this patient and describe its management

DD of abdominal masses

- 60 years old patient presents with a palpable mass in right iliac fossa, describe the diagnosis of such a case
- Describe an approach to suspected pancreatic mass
- Enumerate the possible causes of focal lesion of spleen and how to plan for their diagnosis
- Discuss gastrointestinal submucosal tumors

Abdominal pain

- How to differentiate between different causes of upper abdominal pain

Non cardiac chest pain

Differential diagnosis of nausea and vomiting

Intestinal gas and bloating

References:
1- Manual of gastroenterology: diagnosis and therapy 4th edition
2- GI-liver secrets plus: 4th edition
3- The Washinton manual of gastroenterology: 3rd edition
4- Davidson's principles and practice of medicine
5- Lecture notes of internal medicine: by Osama Mahmoud Mohamed [professor of internal medicine Ain Shams University]
6- Basic gastroenterology and hepatology: by Hussien Abdel-Hamid [professor of gastroenterology and internal medicine El-Azhar university]